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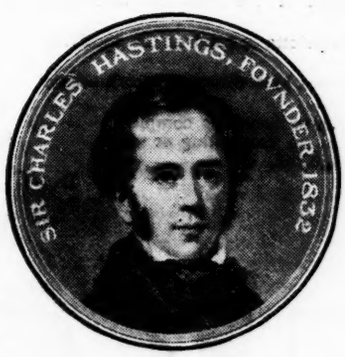

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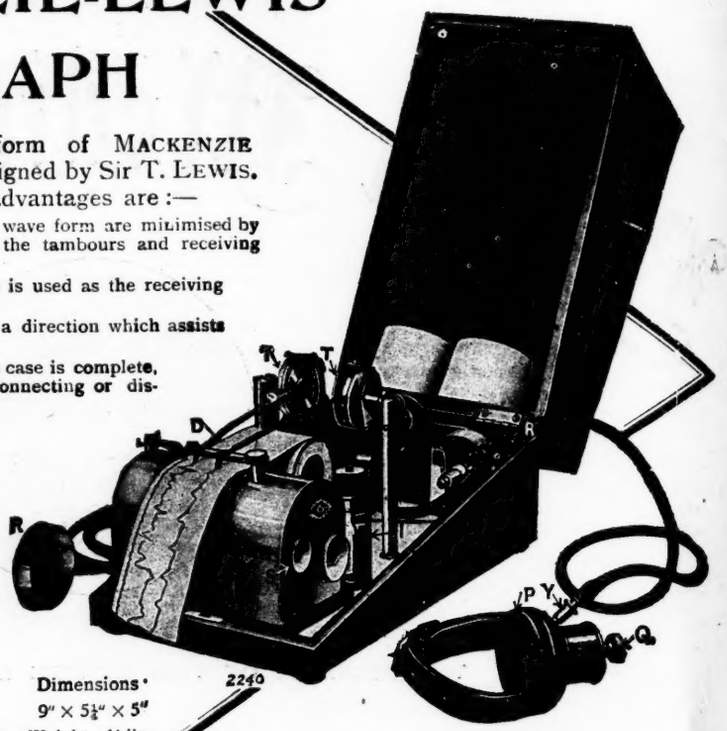

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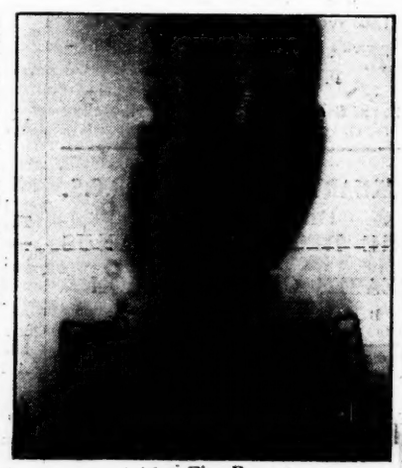

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DISCUSSION ON DEGENERATIVE DISEASES OF THE LIVER.

OPENING PAPER

BY

SIR HUMPHRY ROLLESTON, K.C.B., M.D., D.C.L.,

President of the Royal College of Physicians of London; Emeritus Physician, St. George's Hospital.

Introduction.

THE change that has taken place in the outlook of clinical medicine, from the era of physical signs to that of functional disorder, is reflected by the subject chosen for this discussion—namely, the degenerative diseases of the liver—for the detection of degeneration of the liver in its early stage largely depends on tests for functional efficiency which are not too elaborate to be carried out in hospital practice. It has thus been shown that functional disturbance, such as may be due to degeneration, may occur in the absence of obvious symptoms, at any rate at the time, and thus information is obtained of diminished resistance in, and damage to, the liver, which may be of value as regards the future treatment of the patient. The experiences of the war in the toxic jaundice of munition workers and the increased attention directed to the jaundice following the treatment of syphilis by salvarsan were discussed in the Pathological Section at the 1920 meeting of the British Medical Association (Miller and Rutherford[44]), and the subject of the degenerative diseases of the liver is therefore now ripe for clinical consideration.

The Forms of Hepatic Degeneration.

In discussing the somewhat extensive subject of the degenerations of the liver it is obviously desirable first to determine what are the diseases that may fairly be considered as coming under that heading, and later to refer to their clinical aspects and diagnosis. On clinical grounds it may be well to divide the cases of degeneration of the liver cells into: (1) those that are primary or at least simultaneous with changes in the supporting and vascular tissues of the organ, including Kupffer's cells; and (2) those secondary to (*a*) gross disturbances of the vascular supply of the organ—for example, in portal thrombosis or cardiac failure; (*b*) inflammation or suppuration, as in abscess, pylephlebitis, or cholangitis; and (*c*) biliary obstruction. There is not any distinction to be drawn between the pathological changes in these two groups, but it is to the first group that attention will be almost exclusively directed in the introduction to this discussion. They may be classified as (1) acute and subacute, and (2) chronic.

The primary acute degenerations of the liver cells may be clinically divided into the slight and the grave; the slight often transitory and without any obvious symptoms, though the recent tests for hepatic function may reveal insufficiency of the liver cells. That recovery may occur was proved experimentally by Whipple and Sperry,[79] who produced hyaline necrosis of the central two-thirds of the hepatic lobule by repeated chloroform anaesthesia for one to three hours on successive days. Acute degenerative changes may supervene in a previously damaged liver, as in cirrhosis or in the liver of chronic venous engorgement, and in this latter instance the change has been described as aseptic (Bolton[4]), as due to cytolytic ferments derived from the liver cells (Oertel[50]), or as bacterial (Mallory,[42] Frothingham[14]).

The chronic degenerations of the liver include senile atrophy, fatty change, amyloidosis, cirrhosis, and the cirrhosis of haemochromatosis; the relation of primary carcinoma to degeneration of the liver will also be discussed.

ACUTE DEGENERATIONS OF THE LIVER.

Acute infections and intoxications may produce partial or total degeneration of the lobules of the liver. Zonal necrosis of the hepatic lobule was studied by Opie[52] in 1904; the peripheral zone is seldom affected as it is supplied by the portal vein and the hepatic artery, and poisons are prone to be swept on by the arterial blood into the intermediate zone, causing mid-zonal necrosis; out of 500 cases examined there were 4 only of peripheral necrosis, 3 being associated with puerperal eclampsia. Mallory,[42] who previously described two forms of necrosis—focal and diffuse or central—found the latter to be specially connected with streptococcic infection; and more recently the central zone, which from its poor blood supply is the most vulnerable, has been found to be earliest and most affected in tetrachlorethane, trinitrotoluene, and arsenobenzol poisoning (Turnbull[75]). Combined necrosis of the middle and central zones is, as Opie pointed out, an early stage of the process that terminates as acute yellow atrophy.

Acute parenchymatous degeneration or cloudy swelling of the liver cells, such as occurs in various fevers, infections, and intoxications, is the effect of a process either less virulent generally or with less selective power to act on the liver. It may be the first sign of degeneration which subsequently shows fatty or necrotic change, or it may not proceed further and be followed by recovery of the liver cells. There are thus these three grades, or perhaps it would be safer to say three forms, of degenerative change. How far cloudy swelling is concerned in the production of symptoms in fevers and intoxications is an interesting question on which information is required and may be provided by functional tests, and it is possible that its importance has been overlooked in the past, even as regards the production of acidosis.

Acute and subacute hepatitis show in a varying degree, which may be regarded as depending on the nature of the causal agent, the attempts to repair the accompanying cellular degeneration—namely, cellular regeneration and proliferation of the interstitial connective tissue. It may be suggested that those forms of hepatitis that from the start are characterized by well-marked regeneration are less prone than the forms showing mainly degeneration to be followed by cirrhosis. Thus it is remarkable how very rarely cirrhosis can be ascribed to malarial hepatitis in which regeneration of the liver cells is a prominent feature. It is true that Jonesco and Popper[29] have recently described a malarial hepato-splenic cirrhosis, but they adopt Chauffard's[7] explanation that it is due to poisons derived from the spleen, a process analogous to Banti's disease and Egyptian splenomegaly (Richards and Day[58]), in which hepatic cirrhosis eventually supervenes. It will be interesting to hear if cirrhosis is a sequel of spirochaetosis icterohaemorrhagica, in which well-marked regeneration of the liver cells may be present microscopically; at present there does not appear to be any evidence of this. On the other hand, Leonard Rogers[60] has shown that cirrhosis follows kala-azar and amoebic dysentery, in both of which degenerative rather than regenerative changes are seen in the liver cells. Possibly the connective tissue proliferation, which Nathan[48] argues serves a useful purpose as a nutrient medium for the liver cells, is only called into being when the liver cells fail to regenerate and proliferate without this help.

The grave acute degenerations of the liver provide the cases of the rather ill-defined clinical condition of icterus gravis, forms of which may be roughly catalogued as: (1) Acute yellow atrophy of inconstant or unknown etiology, usually sporadic, and characterized by naked-eye atrophy of the organ, extensive necrosis, and subsequent autolysis of the liver cells. If not immediately fatal, it is succeeded by the process variously described as subacute atrophy, multiple nodular hyperplasia, acute cirrhosis, nodular hepatitis. (2) Due to known infections, such as streptococci, *Treponema pallidum*, *Leptospira* (*Spirochaeta*) *icterohaemorrhagiae*, *Leptospira icteroides* of yellow fever, in which gross atrophy and autolysis are not in evidence. (3) Due to known poisons, which either produce severe degeneration with necrosis—such as tetrachlorethane, trinitrotoluene, and arsenobenzol (salvarsan) preparations—or well-marked fatty degeneration, as in phosphorus, chloroform, and iodoform poisoning. Some of these will be briefly passed in review.

Syphilis.

Syphilis in its early stage may produce a benign jaundice which is probably due to disordered action of the liver cells and not to intrahepatic and intralobular obstruction. But that this is the sole explanation may from the rarity of this

complication (0.3 per cent.) be questioned; possibly some other factor, such as an infection of so low a virulence that it would not damage a healthy liver, is able to exert this effect in an organ with its resistance already impaired. In exceptional instances, of which Parkes Weber[77] collected 53 cases before the era of arsenobenzol compounds, the lesions of acute yellow atrophy are induced, and here again the question of the sole responsibility of syphilitic infection may be raised. Whether or not the *Treponema pallidum* is present in the liver still requires an answer.

Since the treatment of syphilis by arsenobenzol compounds has become general, the incidence of benign jaundice (0.56 per cent. among 39,377 military cases[65]) and of acute yellow atrophy has increased. The occurrence of such cases in groups and sometimes in association with epidemic jaundice or other infection (Stokes, Ruedemann, and Lemon[71]) in the neighbourhood has lent support to the natural suggestion that infection is the additional factor responsible for jaundice in syphilitic patients undergoing arsenobenzol treatment—an attractive but so far unproved explanation. The whole subject has been much discussed, and the Salvarsan Committee of the Medical Research Council has issued one report and has in the press another (Special Report Series, No. 66), which contains information on as yet unpublished work done by Mackenzie Wallis on functional tests—the laevulose tolerance and the blood lipase—showing that temporary hepatic insufficiency almost always follows a course of arsenobenzol injections. Spence and Brett[68] by the blood laevulose test found evidence of hepatic insufficiency in cases of benign jaundice following arsenobenzol treatment, and Widal, Abrami, and Iancovesco[80] obtained positive results in the cases following salvarsan treatment, both without jaundice, and more markedly in cases with jaundice, by their haemoclasic reaction, which, however, awaits further confirmation.

Spirochaetosis Icterohaemorrhagica.

In spirochaetosis icterohaemorrhagica the microscopical appearances show much variation, and jaundice, which is not an essential feature, does not correspond with the degree of structural change; it may indeed be extremely prominent in association with but slight microscopic change, and vice versa (Garnier and Reilly[15]). McNee[40] describes three groups of cases: (1) those with necrosis in the central zone of the liver; (2) those showing regenerative changes in the liver cells which are separated from each other and contain bile pigment, but have not undergone necrosis; (3) those with little change. The jaundice has been regarded as obstructive or as haemolytic (Basile[3]), but Brulé[6] and McNee consider it to be due to disordered function of the liver cells. Spirochaetosis icterohaemorrhagica is an example of the syndrome of hepato-renal insufficiency or of the cases otherwise described as acute nephritis with jaundice or hepato-nephritis, in which both organs are affected by the causal agent, and thus differs from cases in which the kidneys undergo degenerative changes from the intoxication due to grave hepatic lesions. The prognosis of cases of icterus gravis is in great measure determined by the functional activity of the kidneys, and this is particularly so in spirochaetosis icterohaemorrhagica, in which grave symptoms may be due to uraemia. Garnier and Reilly[16] indeed contrast the gravity of spirochaetosis icterohaemorrhagica, which they regard as depending on renal insufficiency, with that of acute yellow atrophy, which is due to hepatic insufficiency.

Toxic Jaundice.

During the war 100,000 persons in this country worked in *trinitrotoluene*, and among them 404 cases of toxic jaundice were reported to the Home Office (O'Donovan[49]); but after preventive measures were introduced, as the result of the late Benjamin Moore's[45] demonstration that the absorption of trinitrotoluene took place through the skin, the incidence of jaundice fell in a remarkable manner. The outbreak was fully investigated under the auspices of the Medical Research Committee, and two valuable reports ([45] [49]) were issued. A noteworthy point was the latency shown in the onset of jaundice—namely, the long interval that might elapse between the last exposure to the poison and the onset of jaundice, even up to nine months (E. E. Glynn); there was evidence to show that serious damage to the liver might occur without any symptoms (Panton[49]). The causation of the hepatic changes—which, like those of tetrachlorethane and salvarsan poisoning, are much the same as those of acute yellow atrophy—has given rise to some discussion. Benjamin Moore argued that trinitrotoluene first attacked the blood, and that from the resulting excessive metabolism of haemoglobin the liver became exhausted and underwent the grave degenerative lesions. Panton[49] disputed Moore's statement of constant blood destruction, and it may be added that if excessive haemolysis so exhausted the liver as to lead to grave lesions this should occur in pernicious and other forms of severe haemolytic anaemia. Though it was very difficult to induce the hepatic lesions in experimental animals by trinitrotoluene, the changes in the liver were regarded as due to the direct action of the poison on the hepatic cells. But from the comparative infrequency of toxic jaundice and from its tendency to occur in outbreaks the existence of some additional factor, such as a coliform infection, harmless or trivial in its effects on the healthy liver, but capable of producing grave changes in a liver with its resistance lowered by prolonged exposure to trinitrotoluene, has naturally been suggested. But no definite proof of this could be obtained. The position is exactly the same as regards the hepatic lesions seen after the administration of arsenobenzol compounds, and in both the factor of individual want of resistance on the part of the liver is a possible explanation.

On the histological evidence H. M. Turnbull[49] regarded the jaundice as obstructive and not haemolytic in nature, but he admitted that the escape of bile into the blood as the result of parenchymatous disintegration could not be excluded. Workers absorbing trinitrotoluene pass a chromogen, derived from trinitrotoluene in the urine, which is detected by Webster's test; but with the onset of toxic jaundice the chromogen disappears, and Dale[49] shows that this azoxy compound is the most satisfactory method of eliminating trinitrotoluene from the body. So although a positive Webster test shows that the individual is absorbing trinitrotoluene its disappearance should be regarded as a danger signal of toxic effects.

Tetrachlorethane was employed early in the war as "dope" for rendering the wings of aeroplanes impervious to air and moisture, and in November, 1914, cases of toxic jaundice appeared. Up till July, 1916, when its use was given up, there were in all 70 cases of jaundice with 12 deaths (T. M. Legge[33]). In 1913 a few cases had occurred in this country and in Germany. This form of toxic jaundice, specially investigated by Willcox, Spilsbury, and Legge,[83] was due to the inhalation of the vapour of tetrachlorethane, and both experimentally and in man caused first fatty change in the liver, kidneys, and heart, and then extensive degeneration of the liver cells with diminution in the fat content, so that the lesions resemble those in trinitrotoluene poisoning. Willcox[82] draws attention to the insidious onset of symptoms, the comparatively long duration of the acute stage with deep jaundice (thus differing from acute yellow atrophy), the freedom from much fever (a distinction from infective jaundice), the absence of anaemia, and the well-marked jaundice.

Opie's[53] observation that whereas neither *Bacillus coli* nor chloroform alone produces acute degeneration and atrophy, this lesion may result from their combined action, has an important bearing both on the etiology and clinical aspects of icterus gravis and acute yellow atrophy. Thus it helps to explain the incidence of these manifestations when an anaesthetic is administered during the course of an acute intestinal or other infection. In this connexion the observations of E. A. Graham[19] that the resistance of the liver cells runs *pari passu* with their glycogen content has obviously a practical application: it has been shown experimentally by Davis and Whipple[10] that sugar given before anaesthesia protects the hepatic cells against damage by chloroform, and when given after anaesthesia enables the cells to recover rapidly, that proteins are much less effective in this respect, and that the administration of fats facilitates the changes in the liver cells. On these grounds sugars and carbohydrates should obviously be given before and after operations, proteins sparingly, and fats avoided.

Widespread, if not total, degeneration of the zones of the hepatic lobules without necrosis may be due to poisons such as alcohol, phosphorus, chloroform, and iodoform, and be followed by excessive fatty change. I have seen an intensely fatty liver weighing 10 lb. in an alcoholic woman. Leathes[32] has shown that this extensive accumulation of fat may occur rapidly; and it appears reasonable to regard degeneration of the cells as the cause of the failure of the normal desaturation of fat by the liver, and so of accumulation of fat in the liver. It must, however, be admitted that such pathological fatty accumulation may also be a chronic

condition—for example, in alcoholic and tuberculous patients—and so come in the later category; in determining this point the tests for hepatic efficiency should lead to certain knowledge. The detection by functional tests of the presence of degeneration and fatty changes in the liver before operation would obviously be of value in the prevention of further hepatic degeneration by forbidding chloroform anaesthesia and by emphasizing the need for the administration of sugar.

Clinical Manifestations.

The clinical manifestations of acute degenerations of the hepatic cells vary greatly; in the severe forms there may be jaundice, cholaemia, and other obvious signs of hepatic insufficiency—as in acute yellow atrophy and icterus gravis; on the other hand, in the slight cases jaundice may be absent, and it is only by means of tests for hepatic insufficiency that the existence of impaired function of the liver can be established. The clinical latency of acute degeneration of the liver cells is suggested by two events: (*a*) the occurrence of acute symptoms a considerable time after exposure to the responsible poisons, such as trinitrotoluene and arsenobenzol preparations; and (*b*) the evidence of hepatic insufficiency revealed by efficiency tests—the blood laevulose and the lipase tests—after courses of salvarsan. To explain why symptoms do not appear at once when acute degenerative changes have presumably occurred, it may reasonably be suggested that the initial degeneration is not sufficiently widespread to exhaust the compensatory power of the liver, and in support of this the well-known cases of subacute atrophy may be instanced.

The delayed occurrence of acute atrophy in persons removed from exposure to trinitrotoluene, or in patients weeks or months after the termination of a course of salvarsan, is a difficult problem; three explanations may be tentatively mentioned: (*a*) A bacterial or other poison derived from the intestine or elsewhere may attack the liver cells, which, being already damaged, are not able to offer effective resistance to a poison against which they have no acquired immunity. It appears probable that the influence of two poisons acting successively on the cells and tissues of the body has hardly received due attention, though Opie's work has thrown light on this subject. Stuart McDonald[39] suggested infection with organisms of the coli-typhoid group, acting on a liver damaged by syphilis and by salvarsan, as the additional factor responsible for the occurrence of the grave hepatic lesions following treatment by arsenobenzol compounds, but Turnbull's[75] histological examination of the livers in 8 cases did not lend any support to the view of bacterial infection. (*b*) Foulerton[18] pointed out that chloroform, ether, and tetrachlorethane are fat solvents, and that three other substances which produce degenerative changes in the liver—phosphorus, dinitrobenzol, and trinitrotoluene—are readily soluble in fats. He suggests that these poisons become linked with the reserve fats in the subcutaneous and visceral adipose tissue, and when on an emergency these fats are mobilized in considerable quantities and carried to the liver to be desaturated and converted into available organic fat, these poisons pass to the liver in such quantities as to set up grave lesions in an already damaged organ. In conjunction with Hewitson he found that arsenic is present in the largest quantity in those parts of the body that are richest in fat. (*c*) The action of the poison may be progressive, and finally the lesions may become so extensive that complete hepatic insufficiency results; Turnbull[75] considered that in the livers of arsenobenzol and trinitrotoluene poisoning there was strong evidence of the progressive action of the poison.

In degeneration of the liver the multiple functions of its cells are, at any rate from a clinical point of view, less impaired than might have been anticipated; indeed on this point our knowledge is probably more deficient than is generally recognized, and should be greatly extended by the wide employment of the recent tests for functional efficiency. But in connexion with these functional tests the share taken by other parts of the body, such as the pancreas and muscles, must be borne in mind. The most obvious defect is jaundice due to retention of bile pigment in the circulation as the result of disordered function of the liver cells, the bilirubin being shunted into the blood or lymph capillaries instead of into the bile capillaries. But even here we are not on sure ground, for it is no longer certain that the liver cells manufacture the bile pigment; Brulé[6] argues that the liver cells merely pick out bile pigment and salts from the blood and excrete them; and it has been thought that bilirubin is manufactured by the vascular endothelium generally and by Kupffer's cells in the liver (Lepehne[34]; Hatiéganu[23]; C. M. and B. B. Jones[28]) and then passed on to the liver cells, which, possibly after altering the bilirubin in some way, excrete it into the bile capillaries. It is thus possible that the liver cells modify the bilirubin in a manner analogous to their action on fats as described by Leathes.[32] Dr. J. W. McNee has suggested to me that this hypothetical action of the liver cells may account for the form of bilirubin which gives the direct or immediate reaction with van den Bergh's diazo-test of the blood serum[41 76] (in mechanical or obstructive jaundice), and that the delayed or indirect reaction with van den Bergh's test is given by the form of bilirubin (in haemolytic and non-obstructive jaundice or Lepehne's functional jaundice) which has not undergone this modification by the liver cells.

Dissociated jaundice in which either bile pigment or bile salts, but not both, are retained in the blood stream as the result of disordered function of the liver illustrates the diverse, almost capricious, manner in which the degeneration of the liver cells may show itself. Here again we are reminded of the imperfect state of our knowledge, for although Grigaut[21] believes that the cholesterol yields cholalic acid, and that functional disorder of the liver cells interferes with this transformation and so leads to an increased cholesterol content in the blood, the mode of formation of bile acids is far from established. Discussion may perhaps be directed to the view recently put forward by C. M. Jones[27] that the lowered haemoglobin content in the course of acute infections such as pneumonia, enteric, scarlet fever, and septicaemias, and also in chronic degenerative conditions such as cirrhosis, Banti's disease, and hepatitis, is not due to haemolysis but to failure of the liver to resynthesize the derivatives of bilirubin—namely, urobilinogen and urobilin—with the iron into haemoglobin, and that as a result there is an excess of bile pigments obtained by aspiration from the duodenum.

The manifold proteolytic functions of the liver cells depend upon a number of ferments, and, although little is known of those concerned with the metabolism of cystin, alkapton, and the porphyrins, it would seem that these ferments, whether they be confined to the liver or not, must be highly resistant, because the manifestations of cystinuria, alkaptonuria, and porphyrinuria, which Sir Archibald Garrod has happily called inborn errors of metabolism, are so rarely seen even in very grave and extensive degenerations of the liver cells. As a rare example, Simpson's[67] description of haematoporphyrin in the faeces of a case of malaria may be quoted. Non-diabetic acidosis is often associated with fatty liver—for example, in cyclical vomiting, pregnancy, appendicitis, cholecystitis, and delayed chloroform poisoning—because the ketone acids liberated in the de-aminization of the amino-acids are not oxidized. A question for discussion arises as to the causation of the general haemorrhages seen in grave degenerations of the liver; they may be due to diminution in the fibrinogen in the blood from damage to the liver cells, and in support of this there are observations showing that chloroform and phosphorus poisoning and cirrhosis are accompanied by a fall in the fibrinogen content and the coagulation power of the blood (Whipple, Gram[20]). But the poisons or infections responsible for the hepatic degeneration, such as arsenobenzol preparations, may act as acute endotheliolytic agents, and so directly cause haemorrhages; or toxins absorbed from the intestines may, from failure of the liver to stop them, pass into the general circulation.

Prognosis.

The prognosis of cases in which recovery from clinically severe acute degeneration of the liver has occurred and in which the liver has presumably undergone permanent damage, such as subacute atrophy with cirrhosis and compensatory hyperplasia, is a subject on which more information is desirable; for trinitrotoluene poisoning must have left a legacy of many cases of this kind, and others will arise from time to time from non-fatal sporadic acute yellow atrophy and from the ill effects of salvarsan treatment. Rous and McMaster's[63] experimental work showing the great reserve power of the liver both in structural reparation and in function, and the knowledge that ordinary multilobular cirrhosis may become compensated and remain latent, make it probable that in favourable circumstances—namely, freedom from renewed intoxication and secondary infections—the outlook should be fairly good. M. Stewart[70] followed up 17 patients two to three years after recovery from toxic jaundice due to trinitrotoluene, and found that they all were in reasonably good health and had been free from any relapse of

jaundice, but that practically all of them suffered from a certain amount of epigastric pain.

The *treatment* of acute degenerations of the liver, especially from the point of view of prophylaxis, by increasing the resistance of the liver cells by dietetic measures—namely, the administration of carbohydrates—as shown experimentally by Davis and Whipple,[10] has been briefly mentioned above.

CHRONIC DEGENERATIONS.

The *senile atrophy* of the liver with diminution in the size of the lobules and of the cells which contain granules of a so-called liprochrome pigment is not accompanied, as are most chronic degenerations of the liver cells, by hyperplasia of the interstitial tissues, possibly on account of the general loss of vitality of the whole organ.

Pathological fatty accumulation of the liver cells results from degeneration due to infective and toxic processes, and is accompanied by other evidence of impaired functional activity; thus Auld[2] found that blood pigment liberated in the spleen in haemolytic experiments was not stopped by liver cells showing fatty change, though Kupffer's cells were loaded with blood pigment. In normal conditions the blood contains a fat-splitting ferment—lipase—the amount being remarkably constant; in hepatic disease the blood lipase is increased and it has therefore been thought that normally the liver inhibits the formation of lipase. Whipple found the amount of blood lipase increased in experimental chloroform poisoning; he employs a test consisting in the addition of ethyl butyrate to the blood serum as a means of estimating the functional efficiency of the liver. The frequent absence of jaundice in fatty livers shows that the function of biliary secretion is not necessarily affected in a severe manner to correspond with failure in its activity in fat metabolism.

Amyloid liver, which is an infiltration of the vascular framework of the liver, is by definition not a degeneration, but it has as much claim to be mentioned here as the fatty liver, except that the pathological fatty infiltration is secondary to degeneration of the hepatic cells. In the amyloid liver the hepatic cells often show a secondary degenerative change, as evidenced by fat or atrophy, and it is therefore noteworthy that cirrhosis does not occur; possibly, as Kanthack[30] suggested, this depends on impaired vitality of the connective tissues.

Cirrhosis.

Portal or multilobular cirrhosis is the result of attempts to repair the damage done by multiple focal degenerations of the cells in the peripheral and intermediate zones of the lobules. Though this process is usually spread over a long period of time, it is not always chronic, for in subacute atrophy and in poisoning by tetrachlorethane and trinitrotoluene the cirrhosis merits the description acute or subacute. Indeed, acute yellow atrophy and portal cirrhosis are the poles of a process similar in nature, though differing markedly in their rate of progress, with transitional stages such as the subacute diffuse hepatitis described by Symmers.[72] The fibrosis in portal cirrhosis has usually been regarded in the light of cicatricial tissue and as devoid of any useful purpose; but the recent experimental work of Nathan,[48] in implanting the omentum into the kidney and liver, suggests that young connective tissue, by providing the liver cells with a nutrient medium which is effective in proportion as it approaches the structure of the embryonic mesenchyma, favours their multiplication and compensatory hyperplasia. In this connexion it may be remembered that the newly formed connective tissue in hepatic cirrhosis is very freely supplied with vessels from the hepatic artery which is normally responsible for the nourishment of the hepatic parenchyma; in fact, there is in cirrhosis a much freer communication between the hepatic artery and the portal vein than normally (F. C. Herrick[24]). The formation of connective tissue in hepatic cirrhosis, therefore, initiates a means of furthering compensatory hyperplasia, but after stimulating the growth of hepatic cells, even to the formation of adenomas, the fibrous tissue, having accomplished its end, becomes old and no longer of any use; indeed, by cicatricial contraction it does harm, and thus is an example of a compensatory process that fails. The secondary changes succeeding the original degeneration in the hepatic cells in cirrhosis that have been mentioned so far are those of a compensatory nature, but their degeneration leads to the production of de-differentiated cells in which the property of active growth is developed at the expense of the higher functional powers. The bearing of such cells on the problem of tumour formation will be referred to later.

The factor of alcoholism in the production of multilobular cirrhosis, though it must still be regarded as important from its frequency and chronicity, is now recognized as one only of the conditions that may, directly or indirectly, produce focal degenerations followed by repair of the liver. Attention has recently been directed to the part played by syphilis in the etiology of cirrhosis, mainly because the Wassermann reaction is so frequently positive in the subjects of that disease (Symmers,[73] Letulle,[35] Owen[54]). It should be mentioned that as long ago as 1900 J. F. Payne[56] expressed his opinion that multilobular cirrhosis in children was generally due to syphilis, and this appears to be specially applicable to familial cases except those of Wilson's progressive lenticular degeneration, for which Hall,[22] who has collected 63 cases, suggests the name "hepato-lenticular degeneration." In adults alcohol very probably acts at an advantage in a liver with its resistance impaired by syphilitic infection. Tuberculosis, also, has been stated to be a cause of cirrhosis, especially by Roque and Cordier,[61] who regard the ascites of cirrhosis as always tuberculous; but even if this latter view is correct, the infection of the peritoneum might be secondary to, and different from, that causing the degeneration of the liver cells. When focal degenerations in the liver occur as the result of infections and intoxication, hepatic cytolysins should be produced from absorption of their protein and a vicious circle result (Fiessinger[12]). How far this may take place is open to considerable doubt. After repeated anaphylactic shock, Longcope[37] found the livers of experimental animals to be cirrhotic as the result of fibrosis around the necrotic foci.

The glycogenic function of the liver has for many years been tested by the examination of the urine after the ingestion of 100 grams of some form of sugar—such as cane, grape, or galactose—by the mouth; but now the laevulose tolerance test, which should not in health give rise to hyperglycaemia, has superseded tests in which the threshold of the kidney introduces a disturbing factor. Chauffard, Brodin, and Zizine[8] find that active cirrhosis is characterized almost constantly by hyperglycaemia, and generally by the presence of bile salts and urobilin in the urine.

The excess of urobilinogen and urobilin in the urine of patients with cirrhosis has long been regarded as evidence of hepatic insufficiency. The mechanism of the formation of urobilinogen and urobilin has received a number of explanations, and recently the commonly accepted view—the entero-hepatic—has been attacked by Hooper and Whipple,[25] Brulé,[6] and C. M. Jones.[27] According to the entero-hepatic explanation urobilin is formed only in the intestine by the nascent hydrogen liberated as the result of bacterial activities, and the urobilin thus formed partly escapes as the stercobilin of the faeces and is partly absorbed and carried to the liver to be reconverted into bilirubin; but if the functional power of the liver cells is impaired, or if they are overworked by dealing with the blood pigment of excessive haemolysis, some of the urobilin passes into the blood and so into the urine. In place of this explanation it is now urged that there is an intrahepatic formation of urobilin from bilirubin, a valid argument in its favour being that duodenal aspiration—that is, above the intestinal level where bacterial activity would lead to the formation of urobilin—shows the presence of urobilin. Whipple[78] contends that there is no evidence of absorption of urobilin from the intestine. Increase in duodenal urobilin occurs in haemolysis, but is also found in cases of anaemia without any other evidence of haemolysis, and, as mentioned above, C. M. Jones,[27] following Wilbur and Addis,[81] suggests that from impaired function the liver fails to resynthesize the urobilin with iron into haemoglobin, and that hence there results an excess of urobilin in the duodenum and a deficiency of haemoglobin in the blood. This would account for the anaemia sometimes associated with portal cirrhosis when there is no evidence of loss of blood by the bowel, such as may be shown by the benzidene test for occult blood.

The pigmented cirrhotic liver of haemochromatosis—a subject discussed in the Section of Pathology and Bacteriology at the meeting of the British Medical Association last year (vide Dunn[11])—presents several features of interest in connexion with the degenerative diseases of the liver. In cirrhosis some degree of siderosis of the liver cells is common (Kretz,[31] Abbott[1]); and, in opposition to the old view that siderosis of haemolytic origin was the cause of cellular degeneration and cirrhosis, it has been argued by Potter and Milne,[57] and, as the result of repeated transfusion of blood for months in rabbits, by Rous and Oliver,[64] that the primary

lesion in haemochromatosis is multilobular cirrhosis of the liver. That haemolysis is not responsible for the excess of haemosiderin was urged by Meltzer,[43] G. Parker,[55] Sprunt,[69] Garrod and his co-workers,[17] and on experimental grounds by Rous and Oliver, who showed that the distribution of iron in the body differs in haemolysis from that in haemochromatosis. But, nevertheless, the haemosiderin should be regarded as derived from the haemoglobin, though its origin from the iron-containing proteins of the cells of the body has been suggested by Mackenzie Wallis[17] and by Sprunt. It is now generally agreed that iron is retained in the body, especially in the liver, which is normally concerned with the storage of iron and the metabolism of blood pigment. The damaged liver cells are apparently unable to deal with the pigment, which therefore accumulates, with the result that further cell destruction and secondary cirrhosis follow. But the question arises whether the haemosiderin collects first in the liver cells or in Kupffer's cells, which are said to be the main repositories of the pigment (W. G. MacCollum). It may be noted that the cirrhotic liver of haemochromatosis is remarkable for the presence of endarteritis, and that there is a close relation between the vessels and Kupffer's cells. The connexion between injury of the cells of the body and the presence of haemosiderin was noted by Potter and Milne and by Garrod as regards the cutaneous distribution which is on the exposed parts, and by Rous and Oliver in the viscera and atheromatous areas of arteries; but there must be some special factor concerned, for visceral and other lesions are common in the absence of siderosis.

The origin of the pancreatic changes, which when advanced are responsible for the terminal stage of bronzed diabetes, is worthy of discussion; the pancreatic fibrosis is still regarded as secondary to the haemochromatosis, whereas the hepatic cirrhosis is considered to be primary. But as some degree of pancreatitis is commonly associated with hepatic cirrhosis, it might logically be urged that this favours the incidence of siderosis, though, as in the case of the liver, the siderosis leads to a secondary and superadded fibrosis—a vicious circle. The sex incidence of haemochromatosis is remarkable: for two cases only (Abbott,[1] Roberts[59]) have been reported in women out of about 80 recorded cases, Roberts's case showing glycosuria. In this respect it corresponds with primary carcinoma in a cirrhotic liver—another, possibly degenerative, sequel of cirrhosis; out of my 52 collective cases of primary carcinoma in a cirrhotic liver 47 were in males; cirrhosis is of course more frequent in males than in females, but the proportion is probably not so high as 3 to 1, whereas the proportion in primary carcinoma arising in a cirrhotic liver is 10 to 1, and in haemochromatosis 40 to 1.

As ordinary multilobular cirrhosis may be followed by primary carcinoma it is not surprising to find that the same sequence of events may occur in connexion with the cirrhotic liver of haemochromatosis, and indeed appears to be rather unduly frequent; Lochlein[36] collected three such cases in 1907, and at the Pathological Section of the British Medical Association meeting last year Maxwell Telling[74] and Matthew Stewart[70a] referred to two cases that occurred at Leeds and were detected at necropsy only.

The amount of iron retained in the body is enormous and may amount to 40 grams, or eight times the normal quantity (5 grams according to Muir and Dunn[47]); and the liver, which normally contains 20 cg., has been found to have 100 times this quantity. There is some evidence that this is due to diminished excretion by the kidneys and intestines (C. P. Howard and Stevens,[26] McClure[38]); but this retention is not absolute. Although Garrod[17] reported absence of iron in the urine, faeces, and bile, Rous[62] described the presence of haemosiderin in the urine as a diagnostic sign of haemochromatosis. A relative retention of iron over a long period would suffice to lead to the enormous accumulation mentioned above.

The clinical features of the complete disease, bronzed diabetes—namely, the peculiar bronzing differing in some respects from that of Addison's disease, especially in avoiding the oral mucous membrane, the enlarged liver with occasionally prominence of the left lobe, and the enlarged spleen and the glycosuria—were regarded by Potter and Milne as a chain of circumstances which is rarely completed rather than as a definite symptom complex. Garrod,[17] who also inclines to the view that it is not a definite disease, brings out the distinctive features of the pigmentation—namely, its occurrence on parts exposed to the air and light rather than to pressure and irritation, thus showing a resemblance to the pigmentation he has recently described in porphyrinuriacs, and its superior claim to the adjective "bronzed" as compared with that of Addison's disease and of chronic arsenical poisoning. He refers to the somnolence and asthenia as the results of the cirrhosis rather than as due to diabetes. From pigmentation of the ductless glands pluriglandular insufficiency and disappearance of the secondary sex characteristics have been described (Claude and Sourdel[9]). The blood shows hyperglycaemia but no anaemia. Skiagraphically the liver does not show any increased opacity (Shattock[66]), so *x* rays do not help in the diagnosis.

Diagnosis.—The association of glycosuria, hepatic cirrhosis, and cutaneous bronzing makes recognition easy; but glycosuria is usually a late event. In cases of cirrhosis with cutaneous pigmentation examination of a piece of skin may clinch the diagnosis by showing the presence of haemosiderin microchemically, and the discovery of the pigment in the urine has a similar significance; but negative results with these tests are not of any value.

Primary Carcinoma.

Primary carcinoma of the liver is not usually regarded in the light of a degenerative process, but as the result of a proliferation which has run riot. Primary carcinoma following cirrhosis is the form of hepatic new growth in which degeneration would appear to be most likely to play a part, for here progressive degeneration is known to occur and to be followed by compensatory hyperplasia of the liver cells; but according to Muir[46] the most reasonable explanation is that of Orth—namely, that for some unknown reason the proliferation oversteps the normal and takes on the autonomous character of a neoplasm. Thus carcinoma has been regarded as a regenerative process in which the de-differentiated cells have taken over the power to invade and destroy other cells (Broders[5]). But the view that degeneration is the primary step in carcinoma deserves consideration; from the study of senescence in dogs Goodpasture[18] concludes that degeneration, besides leading to the death of some cells, is followed by de-differentiation of others which become simpler in structure and function and recover their earlier power of growth, so that metaplasia and neoplasia are accidents of commencing old age. Oertel[51] also regards the transformation of degenerating into carcinoma cells as a phenomenon of senescence and due to disturbances in the nucleus-plasma relations, specifically the loss of nuclear chromosomes. He argues that of the two groups of chromosomes those with higher functions disappear while those concerned with growth survive, and that hence there develops a race of cells lacking the differentiation of normal cells but endowed with vegetative and reproductive process.

Points for Discussion.

The extensive subject of degenerative diseases of the liver raises many interesting questions, of which the following are a few only.

1. The tests for functional efficiency of the liver; their scope, limitations, and results, especially in slight and latent degenerations of the liver.

2. Is the jaundice occasionally seen in early syphilis, in syphilitic patients after arsenobenzol treatment, and the jaundice of munition workers due to an additional factor—namely, infection—or does it merely depend on inherent weakness of the liver?

3. What is the explanation of the delayed onset of symptoms in persons previously exposed to the action of poisons such as trinitrotoluene and arsenobenzol preparations?

4. In degenerative diseases of the liver is jaundice due to (*a*) failure of the damaged cells to remove from the blood bilirubin formed elsewhere, or (*b*) do the liver cells, as the result of disordered function, shunt the bile pigment into the lymph or blood capillaries instead of into the biliary capillaries?

5. Is anaemia in hepatic degeneration due to failure of the liver cells to resynthesize urobilin and iron into haemoglobin?

6. The intrahepatic formation of urobilin.

7. How far is the incidence of cirrhosis after hepatitis accompanied by degeneration of the liver cells obviated by concomitant hyperplasia of the liver cells?

8. Is the interstitial hyperplasia in cirrhosis initially a beneficial process?

9. The value of haemosiderinuria in the diagnosis of haemochromatosis.

10. The relation of primary carcinoma of the liver to a previous degeneration and de-differentiation of the liver cells.

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DISCUSSION.

Professor HUGH MACLEAN (St. Thomas's Hospital, London) said: Sir Humphry Rolleston has given us such an excellent and concise summary of the present position of liver pathology that I think little remains to be added. Personally, I should like to say something in connexion with liver tests, and more particularly with regard to the new laevulose test. Every investigator who tries to evolve tests for liver deficiency is always confronted with the difficulty that the functions of the liver are not really understood, and consequently it is not easy to suggest suitable methods. The two tests of which I have had most experience are the lipase test and the modern laevulose test. In my opinion the lipase test is, on the whole, not very satisfactory, as it cannot be relied upon to indicate the slighter derangements of liver activity. In certain cases it is useful, but on the whole not very helpful except in gross cases. With regard to the laevulose test, I should like to give its history very shortly, so as to clear up certain possible misunderstandings. The modern laevulose test was first used at St. Thomas's Hospital over three years ago by MacLean and de Wesselow, and afterwards by Spence and Brett; it was based on an observation made by the former observers, which was published in the *Quarterly Journal of Medicine* in January, 1921. This observation was to the effect that whereas all the ordinary sugars such as glucose, cane sugar, lactose, maltose, and galactose, when ingested raised the concentration of sugar in the blood, this did not happen when laevulose was given. Thus, if 50 grams of glucose were given to a healthy person, the blood sugar concentration was increased in the first half-hour or so from the usual 0.1 per cent. to about 0.16 or 0.17 per cent. From this maximum point the concentration began to decrease, and in about one and a half hours the blood sugar had returned to its normal value. When, however, 50 grams of laevulose were given, and the blood sugar was estimated at half-hourly intervals as before, no rise was found to take place. The effects of the two sugars on a healthy subject might be represented graphically by a distinct curve for glucose, and by a straight line for laevulose. From various considerations it was known that this lack of power on the part of laevulose to raise the blood sugar depended on an intact liver, for it was found that in patients suffering from a definite lesion of the liver the laevulose acted more or less like glucose and caused a marked increase in the blood sugar concentration. The modern laevulose test is therefore based on two facts: (1) laevulose, when given by mouth in doses of from 30 to 50 grams, does not raise the blood sugar in healthy subjects with an intact liver; (2) when the liver is defective it is not able to prevent laevulose from entering the blood stream, and so a rise in blood sugar concentration follows the ingestion of this sugar.

I should like to point out that laevulose and nearly all the other sugars have from time to time been used as liver tests, and that laevulose has been specially employed by Strauss. Now Strauss just gave a dose of laevulose and afterwards tested the urine for the presence of sugar. If the urine gave a sugar reaction the fact was taken as indicating liver involvement. It hardly seems necessary for me to point out that the modern laevulose test described has no connexion whatever with Strauss's test, except that in both cases laevulose is used. To say that the tests are in any way similar betrays an entire ignorance of the fundamental basis of the modern laevulose test. One might as well say that two entirely different surgical operations were the same because, in both cases, the surgeon used the same scalpel. A very slight experience of Strauss's test shows that it is of little value. This is fully explained in the light of the results of the modern test. Strauss's test could only give reliable results in gross cases where the renal threshold for laevulose had been exceeded. It is quite common, however, to find a marked sugar reaction with this test in patients in whom the liver is quite efficient, as indicated by the modern laevulose test and by the clinical condition. On the other hand, in many cases of obvious liver involvement no indication whatever of the condition is obtained by Strauss's test. It is quite impossible to enter into the reasons for these discrepancies here, but so marked are these anomalies that the test has long ago fallen into disrepute. The modern laevulose test is based not on Strauss's work, but on the observation already described, that when the liver was intact laevulose would not raise the blood sugar concentration. The test resulted directly from this observation, and until this essential fact was established the blood sugar method could

not be utilized as its results could not be interpreted. Further, it seems certain that in many cases the apparent positive results with Strauss's test were much more intimately associated with impurities in the laevulose than with any liver deficiency.

With regard to the prevention of toxic jaundice after the administration of arsenobenzol, it would appear, from the results of observations made by Colonel Harrison at St. Thomas's Hospital, that the ingestion of some sugar before the injection of the drug was of material benefit in warding off such attacks. In a set of patients receiving sugar before injection there were only two or three cases of jaundice after treatment, while in another set not receiving sugar there were nearly fifty cases. Whether or not a larger experience will justify these results must of course depend on future observations.

Dr. C. M. WILSON (London) said that hepatic insufficiency might be betrayed either by obvious signs or symptoms, such as jaundice, or in the absence of these by laboratory tests demonstrating the latent insufficiency. Clinicians required a test which would apprise them of impaired function of the liver when there were no symptoms to warn them of that impairment, or at any rate before such symptoms appeared. They needed, for example, not so much a test which would tell them the exact extent of the damage that chloroform administered as an anaesthetic had done to the liver, or even the date when that damage had been repaired, but rather one that would veto chloroform as an anaesthetic by warning them of hepatic insufficiency, just as glycosuria arrested the hand of the surgeon. Had we up to the present any such test of liver efficiency? He did not wish to belittle the value of the work done in that field, nor was he blind to the light that by means of these tests was being directed on the multiple functions of the liver cells; but for the moment he was concerned to question whether they possessed any test of liver efficiency sufficiently delicate to tell them what they wanted to know at a time when it was most needed—namely, before the advent of signs and symptoms revealed the nature of the trouble. He would be content in his contribution to that discussion to attempt to find some answer to that question. If he appeared unduly cautious they might, perhaps, agree with him that in chemical pathology at the present time, in its application to clinical work, a conservative view was not without value.

To obtain some idea of the comparative value of such tests, their scope and limitations, he had taken thirty apparently normal male students of practically the same age and carried out on them tests of hepatic efficiency by five methods—the estimation of the lipase and cholesterol of the blood, the laevulose tolerance test, the nitrogen distribution of the blood, and the haemoclasic crisis. Starting from that basis—and in the present confusion in the literature it was necessary to begin by establishing the normal—the same tests were applied to all abnormal conditions of the liver that came under his observation. An investigation of that nature was a laborious undertaking requiring many months for its completion, and he could only furnish them with tentative conclusions. Moreover, the time at his disposal in that discussion robbed these conclusions of their supporting facts, leaving them in the air as a few bald and isolated statements. He would once more remind them that they were seeking for a test whose warning preceded the onset of symptoms. In the course of that discussion a claim had been made that the lipase test satisfied these requirements. This test depended on the increase in certain diseases of the liver of the fat-splitting ferment lipase, which was normally present in the blood. In the thirty students used as controls the figure varied between 0.1 and 0.32. But when the test was applied to diseases of the liver it was found, as Whipple maintained in 1913, that the figure rose only when there was actual necrosis of liver cells. It provided information in certain diseases of the liver, but it did so only when that information had been already furnished by clinical means. The test had little or no value in unmasking a latent inefficiency. And this applied to some of the other tests.

He concluded provisionally that, with the possible exception of the laevulose tolerance test, the only test which gave an early warning of hepatic insufficiency was that described by Widal as the haemoclasic crisis. Under that rather forbidding name was concealed a test disarming in its simplicity. The haemoclasic crisis depended on the fact that the normal digestion leucocytosis was replaced by a leucopenia when the liver was diseased. A white cell count was taken before the patient's breakfast, seven ounces of milk were then drunk, and another count made twenty minutes after the milk. Of thirty normal students more than half showed a rise in the second count of 3,000 or upwards, while only two failed to show a rise of less than 1,000, so that the individual error in the count was not a factor. In two of the thirty the rise was delayed till forty minutes after taking the milk, so that it was advisable to do three counts if the second showed no rise, but commonly only two counts were necessary. In diseases of the liver there was an invariable fall in the second count. The question in this test appeared to be not whether it was positive in the early phases of diseases of the liver, but rather in how many other conditions a fall of the leucocytes followed drinking milk. Since Widal's observation, a certain amount of work had been recorded in Continental journals, recently summarized in *Medical Science*. The haemoclasic crisis was found not only in obvious diseases of the liver, such as carcinoma, but also in the course of certain infections wherein the liver was apparently affected. But it occurred, too, in diseases where the existence of hepatic involvement was either unsuspected or, at any rate, rested on mere speculation. Widal, for example, had found a positive result in asthma and in his (the speaker's) experience the most marked reaction occurred in that malady. He (Dr. Wilson) had also performed the test on 19 epileptics, 18 of whom gave a positive result. It was premature as yet to affirm that the test supplied what they wanted, but from many observations made during the past few months he could testify to its value and to the interesting possibilities that the test opened up. Perhaps the notes of two cases would illustrate in what direction we might look to this test for assistance.

CASE I.

A stout, red-faced countryman attended his out-patient department in May, complaining of epigastric pains. It was not easy to obtain any information through the protecting muscles of the abdominal wall, but he was surprised to find the haemoclasic crisis. The other tests of hepatic insufficiency to which reference had been made failed to support the evidence of the haemoclasic crisis. The physician to whose wards he was admitted could find no cause for the pain, and after a fortnight's observation the man was discharged. The pain, however, continued, and his faith in the test was restored by the reappearance of the man some weeks later with jaundice. The lipase had now risen to 0.83. Laparotomy in July revealed a malignant mass in the region of the pancreas and a smaller tumour in the neighbourhood of the gall bladder.

In this case the test had met the requirements he had put before them in that it furnished information of value in diagnosis before the nature of the illness had been demonstrated by signs and symptoms.

CASE II.

A man of 38 for many months had suffered from a vague malaise. Easily exhausted, he would wake on one or two mornings in the week with a headache and a yellow fur on the tongue. The headache was not severe, and passed off in the course of the morning. He himself ascribed his condition to being "liverish." On the mornings that the patient had a headache he showed the haemoclasic crisis, but on the other mornings he behaved as a normal individual, and showed a digestion leucocytosis. Counts were made on fourteen consecutive mornings. His condition sensibly improved if meat was excluded from his diet. The observation opened up an interesting field of inquiry into a condition which was common and hitherto of obscure causation. Did the liver, acting as a defensive barrier, prove inefficient on the mornings when the haemoclasic crisis occurred?

At that point he was checked by the recollection of his plea for caution, from which he had, perhaps, been temporarily seduced by the interesting possibilities of this test. Real progress lay, not in the application of the test to clinical work, but in the correct interpretation of its meaning and mechanism.

Dr. J. C. SPENCE (London) said: My contribution to the discussion will be limited to a brief description of the laevulose test for liver efficiency, and of its value in the investigation of certain diseases of the liver. I shall dwell more particularly on results I have obtained in cases of catarrhal jaundice. Thereby I shall be able to illustrate how this test can be used as a new experimental method of approach to the further study of liver diseases. I hope to be able to show that the results I obtained in catarrhal jaundice justify me in including this disease among those implied in the title of this discussion—namely, as a true degenerative disease of the liver.

Professor Maclean has already dealt with the principle of the test and the details of the method to be employed in its

use. There is no difficulty in carrying it out, and accurate results can be readily obtained by anyone familiar with one of the newer and more accurate methods of blood sugar examination; 30 to 50 grams of laevulose, according to the weight of the patient, should be given after four to five hours' fasting. These amounts in a normal person will cause no rise in blood sugar. If the liver's efficiency be impaired in any way the sugar brought to it after absorption from the alimentary canal will not be stored in the liver, but will pass through the organ to appear in the systemic circulation, and a rise in the blood sugar content of the blood will result. The height and length of the blood sugar curve, which portrays this rise, will be in proportion to the degree of hepatic inefficiency present. When using the test the possibility of diabetes mellitus must first be excluded, as this disease gives blood sugar curves similar to those of extreme hepatic inefficiency.

[Dr. Spence then showed charts which illustrated results he had obtained in normal people in cases of toxic salvarsan jaundice of various degrees of severity, and in cases of obstructive jaundice due to impaction of a stone in the common bile duct.

Fig. 1 illustrated the result in a normal person. After 40 grams of laevulose there was no appreciable rise in blood sugar. The results obtained in various diseases of the liver he classified as moderate, severe, and extreme degrees of liver inefficiency, according to the height of the curve.

Fig. 2 indicated a moderate degree of liver inefficiency in a case of toxic salvarsan jaundice. After 50 grams of laevulose the blood sugar percentage varied from 0.090 to 0.126 after half an hour, to 0.148 after 1 hour, to 0.137 after 1½ hours, and to 0.112 after 2 hours.

Fig. 3 showed a severe degree of liver inefficiency in a man who developed jaundice after an injection of N.A.B. After 50 grams of laevulose the blood sugar percentage varied from 0.125 to 0.137 after half an hour, to 0.192 after 1 hour, and to 0.154 after 1½ hours. In this case the rise of blood sugar was higher and more prolonged than in the former.

Fig. 5 showed the result in an extreme case of liver inefficiency. The blood sugar percentage was 0.117, 0.150 after half an hour, 0 141 after 1 hour, 0.161 after 1½ hours, 0.192 after 2 hours, and 0.184 after 2½ hours. This was a significant result in an important case, and required more detailed comment. It was a case of a man, aged 57, who developed jaundice after two courses of silver salvarsan. The test was carried out in the third week after the appearance of the jaundice. At that time his symptoms suggested only an attack of moderate severity, with a correspondingly good prognosis. The result of the test led to suspicion of a greater degree of liver damage than the clinical manifestations showed. These suspicions were confirmed. Two days later the patient passed into a condition of cholaemia and died. *Post-mortem* examination revealed extreme toxic necrosis of the liver.]

In applying the test to these cases of salvarsan jaundice my experience has led me to formulate this working rule: If the laevulose test produces a blood sugar rise of 50 mg. per 100 c.cm. (for example, from 0.110 to 0.160 per cent.) which does not fall to the normal level within one and a half hours, the case must be regarded as serious and requiring the most careful treatment, however slight the other clinical manifestations may be. The following result represents the findings in a typical case of pure obstructive jaundice, due to the impaction of a stone in the common bile duct. After 50 grams of laevulose the blood sugar levels were 0.110 per cent., 0.116 per cent., 0.133 per cent., and 0.120 per cent. This indicates only a slight degree of liver inefficiency, in spite of the fact that the patient was very deeply jaundiced. By contrasting the results of the test in typical conditions of toxaemic or in the hepatic jaundice with those of obstructive jaundice, it will help us to approach the problems of other diseases the pathology of which is not so clear. Catarrhal jaundice is such a disease, for the reason that the opportunities for *post mortem* examinations are so rare.

The results of the laevulose test in cases of catarrhal jaundice which I investigated, showed that a very severe degree of liver inefficiency was present at an early stage of the disease before marked jaundice was present. The recovery of hepatic efficiency in these cases was very rapid, and in some cases was very evident before the jaundice reached its height. Taking into account these two facts, that there is marked hepatic inefficiency during the first few days of the disease, and that this inefficiency, as shown by the laevulose test, is much greater than that usually found in pure extrahepatic obstructive jaundice, it is reasonable to believe that the actual pathological change is one affecting primarily the liver cell, and probably of the nature of a hepatitis. This view, that catarrhal jaundice is an affection of the liver tissue of the nature of a hepatitis, and not an inflammatory obstruction of the common bile duct, is supported by two clinical phenomena which are almost constantly associated with it. These phenomena are the enlargement of the liver and spleen. In some cases the liver reaches the umbilicus, and the spleen is palpable well below the costal margin. This enlargement of the liver is present early in the disease, when, as I have shown, the liver inefficiency is at its height. This early enlargement of the liver is well illustrated in those cases which are often admitted to children's hospitals with a history of fever, vomiting, and drowsiness. Clinical examination reveals only an enlarged liver, and the presence of acetone bodies in the urine. *Faute de mieux* the diagnosis of "acidosis" is made. A few days later jaundice develops, and the diagnosis is now changed to one of catarrhal jaundice. In these cases, at any rate, the enlargement of the liver precedes the appearance of the jaundice, and would confirm the view I have put forward that the condition is probably a hepatitis.

In conclusion, I can but comment on some aspects of the scope and value of the laevulose test. Its chief value is that its results are quantitative. It measures something, whether it be total hepatic efficiency or merely the ability of the liver to store carbohydrates. This being so, its main use will be as a new experimental method with which to approach the problems of liver diseases. Without being as yet in a position to give you a definitive opinion of the comparative value of this test with van den Bergh's test, and Widal's "haemoclasic crisis" test, I hold at present the view that its results give more direct evidence of the condition of hepatic efficiency than do either of these other tests, from which the evidence obtained is largely circumstantial. The laevulose test is of clinical value in controlling the administration of salvarsan. By its routine use between the successive courses of treatment a latent damage of the liver can be revealed. Further treatment could then be modified according to the results of the test. It is a useful aid in the differential diagnosis of toxaemic from obstructive jaundice if it be remembered that very mild cases of the former and very extreme degrees of the latter are likely to give anomalous results. Its ultimate scope has yet to be determined. But it will serve a most useful purpose if, after having added a little to our knowledge, it follows the law of evolution, which affects all clinical methods, and is replaced by a still better test of liver function.

Dr. J. W. McNEE (University College Hospital, London) said: Sir Humphry Rolleston, in opening the subject set down for consideration to-day, has indicated its scope and suggested some lines along which discussion might be profitable. Some of them will be fully dealt with by those who have specially worked on such parts of the subject, and for this reason I have thought it best to take up briefly some rather general but fundamental questions which influence greatly the study of degenerations of the liver, but which are less likely to be covered by other speakers.

Let me begin by saying that, to understand the various kinds of damage which may affect the liver, it is obviously essential to know the structure of the normal organ. It seems, in a way, extraordinary to have to admit that the fine relationships of the structures forming the liver lobule are by no means completely worked out. Our main lack of knowledge is concerned with the intimate connexions between the blood capillaries of the portal vein, the polygonal cells, and the finest bile capillaries. We do not know for certain, although it is commonly inferred, whether any substance, in passing from the vascular capillaries to the bile ducts, must pass through the protoplasm of the polygonal cell. Yet for a complete understanding of the normal and abnormal metabolism of bile pigment such knowledge is essential. The accepted views of the structure of the liver lobule mostly date from the old days of gelatin-carmine injections, some of the best and most widely quoted of which were carried out by Lionel Beale in London as far back as 1856. It is easy to inject and trace the vascular capillaries, but impossible to inject the blindly commencing bile capillaries. All I wish to say here is that I have repeated such injection experiments and made use of other more modern methods of staining, and am unable to confirm some of the descriptions which have crept into most text-books of normal histology. We do not know whether all the glandular cells of the liver lobule have the same function or if they all act together. Various observers have described in some of the lower animals two distinct types of cell within the same lobule, differing in size and in the characters of the contained granules. In a bat, known as *Rhinolophus hippocrepis*, the difference is stated by Oppel to be very obvious

indeed, collections of large clear cells lying amidst groups of smaller, coarsely granular cells. I have in the past two years examined sections from a wide variety of mammalian, avian, and reptilian livers obtained from the London Zoological Gardens, but have never seen more than minor and easily explained differences in the types of cell.

With regard to the functions of one element of the cellular structure of the liver lobule, our knowledge has greatly increased, chiefly as a result of experimental work. This knowledge is of great importance in connexion with the interpretation of the results and signs of many hepatic diseases. I refer of course to the so-called star cells of von Kupffer, large endothelial cells which lie along the walls of the vascular capillaries. In birds these cells form an almost complete lining to the capillaries of the outer part of the liver lobule. In man they appear less numerous. The great importance of these endothelial cells in the metabolism of bile pigment has now been fully recognized, and it seems improbable that the polygonal glandular cells of the liver are concerned in bile pigment metabolism, except in a secondary way. In birds, where the Kupffer cells are extremely numerous, the whole process of bile pigment formation can be watched under favourable experimental conditions. If, for example, blood destruction be induced experimentally in birds, the Kupffer cells may be seen to contain at one and the same time, (*a*) red blood corpuscles in process of disintegration, (*b*) bile pigment, which in birds is the bright green biliverdin, and (*c*) the iron-containing part of the haemoglobin molecule—haemosiderin—which gives the characteristic blue reaction with potassium ferrocyanide and dilute hydrochloric acid. Under such circumstances I have never seen anything suggesting bile pigment within the polygonal liver cells, but only in the Kupffer cells, and again in the bile capillaries. I have stated that in birds the Kupffer cells in the liver are much more numerous than in man, and I have published work in favour of the view that in man the great development of the spleen as an organ must be taken into account. I believe that the endothelial cells of the spleen have in man taken on part of the same function as the Kupffer cells in the liver. In birds the spleen is relatively very much smaller than in man when compared with the liver. This view of a combined action of the endothelial cells of the spleen and Kupffer cells of the liver in the metabolism of bile pigment has now received wide recognition on the Continent, and is fully accepted in a large monograph recently published by Eppinger and others, who deal with the group of diseases such as acholuric jaundice, etc., under the title of "The Liver-Spleen Diseases" (*Die Hepatolienalen Erkrankungen*).

Briefly put, the views which I at present tentatively hold with regard to the metabolism of bile pigment are as follows—these are not original views, and have been supported in whole or in part by others: I believe that in man bile pigment is normally formed in the endothelial cells of the spleen and liver (Kupffer cells), and probably (although this is unproved) passes through the glandular cell to reach the bile capillary. Sir Humphry Rolleston has spoken of a possible explanation of the two kinds of bilirubin described by van den Bergh on the supposition that the pigment is modified in some way in its passage through the polygonal cell of the liver. If the liver cell be damaged or degenerated, the bile pigment, formed in the endothelial cells, may not be taken up by the polygonal cells, with the result that the bilirubin passes on into the blood with the ultimate production of one variety of clinical jaundice. The production of bile pigment by the endothelial cells is probably one of the last functions to cease in hepatic degenerations, and—for example, in acute yellow atrophy of the liver—the vascular capillaries may appear intact when the polygonal cells are largely necrosed.

I may now summarize briefly my ideas concerning the occurrence of jaundice in acute diseases of the liver. If the view I have put forward with regard to the functions of the endothelial cells of liver and spleen be correct, then it would appear possible for icterus to arise under three sets of circumstances:

1. Where there is direct obstruction to the outflow of bile—for example, gall stones blocking the common bile duct.

2. Where there has been increased haemolysis in the body and an excess of bile pigment is formed in the endothelial cells. This excess may be more than the liver cells can deal with, and the excess passes into the blood and may result in icterus—for example, acholuric jaundice, icterus neonatorum, the "latent icterus" of pernicious anaemia, etc. Such an icterus might be expected to be of light degree and symptomless.

3. Where the glandular cells of the liver are damaged, while the endothelial cells continue to functionate normally. In such circumstances one must suppose the liver cells unable to take up in whole or in part the bilirubin offered to them, which therefore has to pass on along the blood capillaries into the circulation—for example, the toxic jaundice of typhoid fever and pneumonia, associated with cloudy swelling of the liver cells; so-called catarrhal jaundice, with acute hepatitis; "late" or delayed jaundice after salvarsan, etc.

In cases like acute yellow atrophy, where in addition to necrosis of many cells the whole liver lobule is finally disorganized, the exact mechanism and type of the icterus is less easy to suggest, and may probably vary at different stages of the disease.

Turning now to some other points in connexion with acute degenerative lesions of the liver. It is evident that far too much attention has been paid to the presence of visible jaundice as a diagnostic sign of acute hepatic disease. It is here that functional tests may be of value in indicating hepatic derangement in the absence of jaundice, especially if the results of the tests can be correlated with the symptoms and signs in the patient. It is not difficult to imagine that different parts of the manifold functions of the liver may be deranged in different ways and at different times without jaundice appearing at all. This has indeed been recognized to occur in one form of "dissociated jaundice"; and since the recognition of bile pigments in the serum has been made much more delicate by the methods of van den Bergh, we know that latent icterus may be present which is unrecognizable in the skin. Further, a study of the clinical features, and later of the histology, of cases of spirochaetal jaundice, has shown me that it is impossible to correlate the intensity of icterus with the extent of the hepatic damage. Sir Humphry Rolleston has referred to some of my results in this connexion. I have described three types of hepatic lesion in cases of this disease, all showing icterus of moderate severity: those with little histological evidence of damage at all, those in which the cells of the lobule are dislocated and individual cells are necrosed, and those in which there is intense necrosis of the central part of the lobules. In passing I may state that I regard the second type of lesion, which I have seen in other acute hepatic inflammations, as exactly corresponding to the desquamation and necrosis of individual cells seen, for example, in the renal tubules in acute nephritis.

I would like to refer very briefly to another type of hepatic degeneration—the so-called fatty degeneration which is seen so well in phosphorus poisoning. Munk has published work on fatty degeneration, especially of the renal epithelium in cases of "large white kidney," which appears to have a direct bearing on this form of hepatic lesion. Munk would place fatty degeneration as a reaction of the cell to damage, which is greater in severity than that producing cloudy swelling, but less severe and slower in action than that causing actual cellular necrosis. Such a view would bring fatty degeneration into line with other types of degeneration of the liver, the reaction of the damaged cells ranging from cloudy swelling right up to complete necrosis. It is well known that the lesion of acute yellow atrophy is easily distinguished from, for example, phosphorus poisoning by the almost complete absence of fatty degeneration of cells, the essential lesion in the first-named disease being cellular necrosis.

Professor ROBERT MUIR, after stating his appreciation of the very valuable contribution given by Sir Humphry Rolleston to the whole subject, first referred to certain points in the pathology of jaundice. The lesions concerned in its production might be distinguished as affecting (*a*) the bile ducts, (*b*) the liver cells, and (*c*) the blood and extrahepatic tissues. Jaundice due to biliary obstruction was, of course, well understood, but he thought that a lesion essentially obstructive, in the sense that the bile was formed but could not be got rid of, might be located in the liver cells themselves. In some cases of acute toxic jaundice lasting some time, small granules of bile pigment might be found in the liver cells, and this seemed to indicate that the bile pigment was being abundantly formed but could not be passed on to the biliary channels. It was conceivable that such lesions as partial necrosis, dislocation of liver cells, and even marked swelling of the parenchyma, might produce this result. The term "obstructive" should thus be taken in a wider sense than

was usually done. With regard to haematogenous jaundice there were two main questions, which were often not sufficiently distinguished by those who used the term. The first was, Could bile pigment be produced by the cells of other tissues than the liver? The second, Did this extrahepatic formation of pigment ever occur to such an extent as to lead to jaundice when the condition of the liver was normal? The first question could, of course, now be definitely answered in the affirmative—in fact, it appeared to be a common property of cells to be able to split haemoglobin into a moiety of the bilirubin type and an iron-containing moiety. To the second question, he considered a definite answer could not yet be given. It seemed doubtful whether a haematogenous jaundice in the strict sense—that was to say, with normally functioning liver cells—had been produced in experimental conditions. His observations in conditions of haemolysis led him to believe that the haemoglobin was split up within the liver cells as well as in the Kupffer cells, and that the latter, to judge from the amount of haemosiderin within them, played a smaller part in the human subject than in many of the lower animals.

With regard to cirrhosis, the all-important question concerned the etiology, and with regard to this our knowledge was very defective. Classifications might be made on an anatomical or on an etiological basis, but they did not correspond. The hob-nail liver, for example, was often produced by other causes than alcohol, whilst alcohol seemed to produce various types of cirrhosis. Cases of atypical cirrhosis seemed to him to be more frequent in recent years than formerly. In cirrhosis generally the essential factor appeared to be toxic action, with twofold effect: on the one hand, leading to degeneration and disintegration of the liver cells, and, on the other, stimulating overgrowth of the connective tissue—neither of these could be said to produce the other. He did not agree with the suggestion put forward that the interstitial overgrowth was to be regarded as a beneficial process, leading to hyperplasia of the liver cells. It seemed rather to be a case either of simple repair following damage, or of reaction to a slight irritant; and hyperplasia of liver cells occurred to a remarkable degree without any interstitial change—in fact, whenever there was any functional call for it. In regard to haemochromatosis he had practically nothing to add to what he had already published with Professor Shaw Dunn. He considered that there was no doubt that the cirrhosis of the liver preceded the deposition of pigment, and his observations also showed that a similar sequence of events might obtain in the case of the pancreas. He had no experience in detecting haemosiderin granules in the urine in the disease. The method, however, should be tried, as, apart from this and the pigmentation of the skin, there was no means, so far as he knew, of diagnosing haemochromatosis during life. As to the origin of cancer in cirrhotic livers, he maintained his former view that the malignant proliferation was a sequel of the hyperplastic proliferation. Microscopical examination showed that, although de-differentiated cells were present, the cancer cells did not take origin from these, but from the large actively functioning liver cells of the hyperplastic foci.

Sir WILLIAM WILLCOX (Medical Adviser to the Home Office), in continuing the discussion, said:

Toxiphylactic Function of the Liver.

A very important function of the liver which has not been sufficiently recognized is its protective function against exogenous poisons. This property of the liver is exhibited markedly when chemical poisons are taken into the system whether by the mouth or by the blood stream; all that is necessary is for the poison to be absorbed into the blood stream so that it passes by it to the liver. The liver has the property of acting like a sponge retention filter and absorbing the chemical poison. It is thus seen that in almost every fatal case of chemical poisoning the bulk of the absorbed poison is found in the liver if death occurs within a few days. Thus, in the case of arsenical poisoning, if the poison—arsenious oxide, for example—is taken by the mouth, after absorption by the gastro-intestinal tract the poison is carried to the liver and a great part is retained there. Again, if the arsenical preparation such as one of the arsenobenzol derivatives be given intravenously and death occurs within a few days, a large proportion of the poison will be found in the liver. Exactly the same rule holds good for metallic poisons such as mercury or lead, and for organic poisons such as chloroform, phenol, trinitrotoluene, etc. In the case of the alkaloidal poisons this property of the liver is particularly well exhibited, for in fatal cases the greater part of the absorbed poison is found in the liver. In the case of morphine poisoning it has been shown that the liver has the power of retaining a large proportion of the absorbed alkaloid, and the excretion of this absorbed morphine takes place from the liver into the stomach. It is probable that a similar action of the liver occurs in the case of other alkaloidal poisons. This protective function of the liver against exogenous poisons should, I think, be called the "toxiphylactic function" of the liver.

It cannot be claimed that the liver stands alone in possessing a toxiphylactic function, for it is well known that both the spleen and kidneys, and probably the other tissues of the body, have the power of retaining absorbed poisons, but to a much less extent than the liver. The liver in the exercise of its toxiphylactic function suffers often serious damage, and this is shown by the degeneration to which its cells are subject, such as the cloudy swelling and the more advanced condition of fatty degeneration following the effect of these absorbed poisons. In many cases the liver may truly be said to have laid down its life in its endeavour to protect the body from the action of exogenous poisons. For example, in phosphorus poisoning the liver cells may become almost entirely destroyed, and in cases of acute fatal poisoning by salvarsan, tetrachlorethane, trinitrotoluene, etc., such extensive fatty degeneration of the liver cells is found that it is quite clear that the normal function of the liver in the body metabolism must have been destroyed, and in such cases the real mode of death is an auto-intoxication due to loss of liver function, rather than a direct action of the poison in question. It is not only in the case of chemical poisons that the toxiphylactic function of the liver is exercised. Exactly the same result follows, though in different degree, the poisons produced by bacterial or protozoal organisms, or auto-intoxications. Toxic degenerations of the liver are therefore shown from the following conditions:

1. *Chemical poisons*, such as tetrachlorethane, trinitrotoluene, dinitrobenzene, dinitrophenol, arsenobenzol derivatives; inorganic arsenic and antimony compounds, phosphorus, arseniuretted hydrogen, phosphoretted hydrogen, chloroform, phenyl hydrazine, toluylene diamine, and many others.
2. *Bacterial poisons*, such as the toxins produced in enteric and paratyphoid fevers, typhus fever, influenza, pneumonia, streptococcal infections, etc.
3. *Protozoal poisons*, such as the toxins produced in syphilis, yellow fever, spirochaetosis icterohaemorrhagica, kala-azar, amoebic dysentery, malaria, etc.
4. *Auto-intoxications*, such as the changes in the liver found in uraemia, recurrent vomiting, etc.

The Time Factor in Toxic Degenerative Conditions.

The time factor has not, I think, received the attention it deserves in considering the degenerative conditions resulting from the action of toxins. This was well shown in the fatal cases of tetrachlorethane poisoning described in my Lettsomian lectures, 1919. In some of the acute cases an extensive degeneration of the liver occurred followed by death with jaundice. In one fatal case the illness was prolonged over many weeks, and symptoms of ascites and portal obstruction supervened before death. Dr. Spilsbury found, on *post-mortem* examination in this case, marked fibrosis of the liver in addition to fatty degeneration of its cells, the fibrosis, which he termed "replacement fibrosis," having occurred in the areas of the liver in which the cells had undergone necrosis from the effects of the poison. In another case which was seen by me several times ascites and portal obstruction followed the attack of tetrachlorethane jaundice. Paracentesis was performed on the patient twice and he made a complete recovery. Two fatal cases of acute fatty degeneration of the liver due to alcohol have been investigated by me in which the liver was very enlarged and yellow, the cells showing very marked fatty degeneration, exactly as is seen in fatal cases of delayed chloroform poisoning. These cases of acute alcoholic fatty degeneration of the liver are rare, but they are very interesting as showing that in some cases alcohol may act as an intense liver poison like chloroform, phosphorus, etc. It appears that the common form of multilobular cirrhosis usually associated with alcohol is brought about by the comparatively slow action of alcohol in causing degeneration in certain parts only of the lobule of the liver, and the destroyed cells become replaced by fibrous tissue, giving the characteristic histological picture of portal cirrhosis. Under this view the two cases of tetrachlorethane poisoning which developed cirrhosis would be comparable

with the condition resulting from the more prolonged and less intense action of the poison alcohol.

The question has been raised as to whether the jaundice resulting from chemical poisons such as tetrachlorethane, trinitrotoluene, arsenobenzol compounds, etc., may not be really due to some bacterial poisoning rather than to the direct action of the chemical poison. It has been said that only a relatively small proportion of cases of jaundice occurred amongst the workers in the two first-named poisons, and that if the poison had been the cause of the jaundice a higher jaundice incidence would have been expected. I think that the best answer to this question is the clinical evidence. In 1914 I personally examined a large number of the workers exposed to tetrachlorethane vapour, and a large proportion of these were suffering from toxic symptoms, such as anorexia, morning sickness, general malaise, headache, etc., a group of symptoms often called "toxic gastritis." Jaundice was the result of long continuance of these symptoms, and hence occurred in a comparatively few cases, since most of those suffering from early symptoms gave up work for a time, thus preventing the occurrence of jaundice. Dr. W. J. O'Donovan, who very carefully investigated clinically the workers exposed to trinitrotoluene, found that a considerable proportion suffered from "toxic gastritis," though the jaundice cases were comparatively few. The condition is exactly comparable to the effects of alcohol, since, as everyone knows, symptoms of "toxic gastritis" occur for a long period before the definite clinical symptoms of cirrhosis, with possibly jaundice. In the case of the arsenobenzol compounds, symptoms of "toxic gastritis" usually occur during the twenty-four hours following the administration of the drug. These are probably due to impaired hepatic function, and the evidence of fatty degeneration of the liver cells in the acutely fatal cases is sufficiently conclusive in all three poisons. It appears to me that there is no doubt that the toxic jaundice resulting from the action of chemical poisons is due to the direct effect of the poison on the liver, and that bacterial influences are unimportant.

Delayed Jaundice following Salvarsan Poisoning.

It has been suggested that the delayed jaundice occurring after salvarsan poisoning is due to retention of arsenic in the body, and that this retained arsenic only acts on the liver at a considerable period after its administration. It is well known that in trinitrotoluene poisoning jaundice may occur many months after exposure to the poison has ceased. In two cases the period was over nine months. It is also known that in the jaundice cases following trinitrotoluene the urine was found free from trinitrotoluene during the jaundice attack. It is quite clear that the jaundice resulting from trinitrotoluene was due to the liver cell damage (hepatitis) consequent on the trinitrotoluene exposure, and that when the jaundice was present the trinitrotoluene was not at that time exerting its effects. The jaundice was the sequence of the toxic action of the poison on the liver. In the case of arsenobenzol jaundice exactly the same explanation holds good. After a single arsenobenzol administration the urine is after three weeks found free from arsenic, but no doubt some arsenic is deposited in the hair, nails, and epidermal tissues. The liver is then comparatively free from arsenic and the minute amount present cannot have any detrimental effect. The toxic effect of arsenobenzol on the liver occurs within a few days of its administration and if several doses are given there is a summation of toxic effects. These give rise to a degeneration of the liver cells and consequent liver changes which may be included under the term "hepatitis." It is the "hepatitis" resulting from the administration of doses of arsenobenzol compounds which gives rise to jaundice, and, just as in the case of trinitrotoluene poisoning, this jaundice may be delayed for months. In no cases of delayed arsenobenzol jaundice have amounts of arsenic been found in the liver which could at that time have been causing harm to the liver. The small amount of arsenic found in the liver in delayed arsenobenzol jaundice where a prolonged course of the drug has been given are accounted for by the deposition of the arsenic in the epidermic tissues and the gradual absorption therefrom of slight amounts of arsenic which could not of themselves be toxic.

Catarrhal Jaundice.

Dr. Spence, in his most interesting contribution, has pointed out that in catarrhal jaundice there is for a few days definite evidence of impairment of hepatic function, as shown by the laevulose test. I have no doubt that "catarrhal jaundice," as seen in peace time, is exactly the same condition as the "epidemic catarrhal jaundice" which occurred during the war, and which was described by me in the Lettsomian lectures, 1919. The enlargement of the liver and spleen occurs in both of these conditions and the symptoms are identical. The jaundice is due to pathological changes in the liver itself, probably arising from a bacterial infection. The degeneration of the liver cells in catarrhal jaundice may, as in some cases recorded by me, be of such severity as to cause death from auto intoxication and atrophy of the liver; this only occurred in about 0.4 per cent. of the cases of "epidemic catarrhal jaundice" seen in Mesopotamia in 1917. It would be expected that if catarrhal jaundice is hepatic in type it would show a definite impairment of hepatic function, and Dr. Spence's confirmation of this is of great value.

The differential diagnosis between catarrhal jaundice and arsenobenzol jaundice can, however, be clearly made. In arsenobenzol jaundice there is a history of the administration of the drug; there is absence of splenic enlargement; the enlargement of the liver is not always so uniform as it is in catarrhal jaundice—thus the right lobe may be relatively more enlarged than the left in salvarsan jaundice. In both kinds of jaundice the liver diminishes in size considerably during the continuance of the jaundice, but the diminution is usually more marked in the case of arsenobenzol jaundice. In arsenobenzol jaundice the laevulose test for hepatic function remains negative for a longer period, while in catarrhal jaundice Dr. Spence has found that the test only remains negative for about three days. The absolute differentiation is shown by the presence of arsenic in the urine, the hair, and the nails in the case of arsenobenzol jaundice. It is important that in the analysis a reliable method for the detection of arsenic should be employed, such as the electrolytic Marsh-Berzelius test, the organic matter being destroyed by treatment with arsenic-free sulphuric and nitric acids.

Professor M. J. STEWART (Leeds) made the following contribution to the discussion:

Toxic Jaundice due to Trinitrotoluene.

In the discussion on atrophy of the liver at the Cambridge meeting two years ago, brief reference was made to the after-history of a series of cases of toxic jaundice due to trinitrotoluene. The result of that investigation was so striking, as showing the remarkable powers of recovery of the liver from what must have been, in some of the cases at least, a very severe destructive lesion, that I felt that the result of a further "follow up" might be of interest in connexion with the present discussion. Within the past fortnight, therefore, I have obtained information about all of the 17 cases in that series, and I have personally seen 13 of them. They had all suffered with toxic jaundice during 1916 or in the early part of 19.7, so that a period of from five to six years has now elapsed since their illnesses. Twelve patients, including 3 who were dangerously ill (one with a red cell count of less than a million), and 5 others who were deeply jaundiced, are now in excellent health. Five of them have married, of whom four have borne children (one, one, two, and three respectively) without trouble or difficulty of any kind. Only 3 of the twelve now complain of occasional attacks of epigastric pain, although two years ago nearly all of them had this symptom. Of the remaining 5 cases in this series, 2 appear to be really ill—one with gastric ulcer, for which she has already had an operation, the other with severe epigastric pain after food, and occasional vomiting. Neither is at present incapacitated, and the latter especially is well nourished. The other 3 patients are full of complaints, but give a rather unconvincing and incoherent account of their symptoms. Their attitude rather suggests a vague hope of further compensation. No single patient has had any return of jaundice, and none of them have ascites. On the whole I think it may be said that so far as ordinary signs and symptoms are concerned, none of these 17 patients appeared to have suffered from hepatic inadequacy. That a number of them had atrophy of the liver is beyond doubt. At the time of their illness 3 of them appeared, symptomatically, to have the disease in as severe a form as several of those who died, and half of them were deeply jaundiced. No doubt in such cases the liver is now the seat of an irregularly distributed fibrosis, but the after-histories given above suggest that this is a strictly limited and non-progressive lesion, probably a pure replacement fibrosis. It is equally clear that sufficient regenerative hyperplasia of the undestroyed liver tissue has

taken place to render the organ functionally sound. In due time, no doubt, old cases of T.N.T. jaundice will come to the *post-mortem* room, and opportunity will be afforded for studying the anatomy of the healed lesion.

The Cirrhosis of Haemochromatosis.

As Sir Humphry Rolleston has mentioned in his opening paper, one of the many unsettled problems in connexion with haemochromatosis is the relation to one another of the two chief hepatic lesions, siderosis and cirrhosis. The older view, which, however, is still held by many, is that the siderosis is the cause of the cirrhosis. A number of recent writers believe, on the contrary, that degeneration and cirrhosis constitute the primary lesion, and that deposition of haemosiderin occurs in consequence of this. A third group takes the view that "neither factor is causative of the other, and presumably the two are due to some third unrecognized cause" (Dunn). In connexion with this problem there is one aspect of the disease on which I think sufficient stress has not been laid; I refer to its chronicity. The observations of Muir and Dunn, Howard and Stevens, and others have shown that in well-marked haemochromatosis the total amount of iron stored up in the liver and other organs is simply enormous, requiring for its deposition many years at the ordinary dietetic rate of iron intake; Howard and Stevens even suggest forty years as the possible length of time in their case. Now it seems to me unlikely that such a state of affairs could be initiated, and continued, by a degenerative and cirrhotic condition of the liver, whereas a primary siderosis, lasting many years, might very well be the starting point ultimately of the degenerative hepatic changes. From an examination of seven cases of haemochromatosis met with in the *post-mortem* room, and illustrating various stages of the disease, I have endeavoured to ascertain whether or not there was any correspondence between the amount of hepatic siderosis and the degree of cirrhosis. The result may be shown in tabular form:

Cases of Haemochromatosis (all men).

Case.	Age.	Amount of Hepatic Siderosis (Microscopically Estimated).	Amount of Free Iron (Percentage of Dry Weight).	Degree of Cirrhosis (Microscopically Estimated).
1	49	+ + + +	3.78	+ + + +
2	71	+ + + +	2.98	+ + + +
3	51	+ +	—	+
4	51	+ +	1.75	+ +
5	44	+ +	—	+
6	52	+ + + +	4.5	+ + +
7	63	+ + + +	3.6	+ + +

Cases 1 and 2 had primary cancer of the liver.

The result of this examination is to show that the two processes, on the whole, keep pace with one another, but that, if anything, the cirrhosis tends to lag behind the pigmentary deposition. A notable point emerging from this study is that haemosiderin may exist in large amount in liver cells which, apart from the presence of the pigment, appear quite healthy, with large, well-stained nuclei.

Carcinoma of Liver in Cirrhosis and Haemochromatosis.

In a series of 6,000 *post-mortem* examinations made during the past twelve years at the Leeds General Infirmary there were in all 8 cases of primary carcinoma of the liver, an incidence of 0.13 per cent. In 4 cases the tumour or tumours originated in a cirrhotic liver, and in 2 others in an organ which was the seat of haemochromatosis as well. In all there were 149 cases of portal cirrhosis in the series, and the incidence in this group is thus no less than 4 per cent. So far as cancer in haemochromatosis is concerned, I know of three published cases (Rindfleisch, Löhlein, and Achard and Leblanc) and one unpublished (Dunn), in addition to the two mentioned above. Inasmuch, therefore, as the number of recorded cases of haemochromatosis must now be well over 100, it looks as if the incidence of carcinoma in this disease is no higher than in portal cirrhosis generally.

Professor STUART MCDONALD (Newcastle-upon-Tyne) said: I very much regret that I have been unable to hear the whole of the papers given in this discussion owing to my having to take part in the proceedings of another Section. I have had the opportunity, however, of reading Sir Humphry Rolleston's opening paper and am particularly interested in what he said in regard to the grave acute degenerations of the liver which may occur in syphilis and particularly in syphilitic cases treated by arsenobenzol compounds. I am particularly obliged for the opportunity of pointing out a slight error which Sir Humphry Rolleston has inadvertently made with regard to my views on this subject. In a paper which I wrote in the beginning of 1918, and which was published in the BRITISH MEDICAL JOURNAL (1918, i, p. 76), dealing with a group of cases of acute liver atrophy in syphilitic patients under salvarsan treatment, I arrived at some general conclusions with regard to the etiology of the condition. In that paper I made certain suggestions which have attracted some attention, and which have been referred to in the recent report of the Salvarsan Committee of the Medical Research Council (Special Report Series, No. 66). The subject is an extremely difficult and obscure one, and the Committee have been unable to come to any definite conclusion as to the exact part played by salvarsan in the production of acute yellow atrophy. From the evidence they present there can, I think, be little doubt that salvarsan accounts for the increased incidence of jaundice in syphilitic patients under treatment by modern methods. Arising out of my paper referred to above, investigations were conducted in Newcastle on this point, and I am at liberty to state that Dr. R. A. Bolam, who was primarily responsible for the clinical side of the investigation, is also convinced as to the relationship of the jaundice to the salvarsan administration. His opinion may be stated thus:

"In the ordinary course of treatment of syphilis by salvarsan compounds a number of cases of jaundice occur towards the end of the course or within two or three months after its completion. This raises the incidence of jaundice in syphilis considerably beyond what was observed in pre-salvarsan days. If a more intensive course be given, the percentage of jaundice cases rises still higher."

In the case of acute liver necrosis, however, the direct relationship cannot be made out so clearly, and the exact etiology of the condition still remains obscure. The Salvarsan Committee's final conclusion includes a statement "that the poisonous action is possibly dependent for its occurrence on the presence of adjuvant circumstances of a nature as yet unknown." There must be something to account for the extreme rarity of the condition. Considering the thousands of cases of syphilis which have been treated by salvarsan compounds the total number of cases of so-called acute yellow atrophy is extremely small. I have suggested the possibility that the condition only occurs when several factors are working together. It is well known that acute liver necrosis occurred in syphilitic patients in pre-salvarsan days and it appears to me that the syphilitic toxin is an important factor in the process. We know, of course, that certain other toxic agents—as, for example, trinitrotoluene, and possibly certain metabolic poisons—may induce a similar or closely related change in the liver. We are not concerned with these agents in this particular group of cases, but for practical purposes we may fairly, I think, take the syphilitic toxin, and the arsenic, and possibly mercurial factors as constant. I have suggested that the typical phenomena of acute yellow atrophy only appear when still another factor, bacterial infection, acts in conjunction with some or all of the others. In the particular group of cases I described I did obtain evidence of bacterial invasion. Admittedly the evidence is incomplete, as it was only obtained *post mortem*, but similar observations have been made elsewhere, and I am still convinced that in the cases I referred to bacterial infection did play a part in the process. The Salvarsan Committee points out very fairly that in certain cases, or groups of cases, there is a certain amount of evidence, apart from the actual bacteriological findings, that infection may be an important factor. I am of opinion that no final conclusion is likely to be arrived at without experimental work, and I intend to continue my investigations on those lines.

Sir ARCHIBALD GARROD, in summing up the discussion, referred to the observations of Hermann Strauss, published some years ago, upon the effect of diseases of the liver in lowering tolerance for laevulose as evidenced by the occurrence of alimentary laevulosuria after comparatively small doses of that sugar.

DISCUSSION ON THE PROGNOSIS AND TREATMENT OF CHRONIC RENAL DISEASE.

OPENING PAPER

BY

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EVERY medical man interested in the pathology of the renal system will probably agree that the subject of chronic renal disease presents problems that are as difficult and obscure as any arising in the whole field of clinical medicine. Many of our older views of kidney disease have gradually changed in the light of modern knowledge, and we can now obtain a very good idea as to the general state of the renal efficiency in any given patient, but the problem of prognosis, and particularly that of treatment, still bristles with innumerable difficulties.

Much has been published recently on the various aspects of renal disease, but I do not propose to enumerate the different opinions expressed, since this would take too long, and at best could only be a summary of very diverse views and conclusions. Instead of this I propose to give you certain conclusions, based chiefly on the results of a large scale experiment carried out on patients obtaining pensions for nephritis from the Ministry of Pensions. In 1919 an arrangement was made with the Ministry by which all patients in one of the London areas should be carefully examined at intervals, and the results obtained from time to time noted for comparison. This investigation was made possible by the Medical Research Council, which was good enough to furnish the necessary equipment and cards. This experiment has now gone on for three years, and it is hoped that it will ultimately furnish data on which the principles of prognosis may be established with some accuracy. Already many interesting points have come to light, but it will, of course, take several years before the full fruits of this investigation can be obtained. Already over 17,000 complete examinations have been carried out and the results tabulated, while several patients have been under observation for nearly four years.

Before passing on to a detailed discussion of prognosis and treatment, it is necessary to give a short account of the different varieties of chronic renal disease. In this connexion I wish to make it quite clear that I do not intend to enter into the problem of the histological appearances of the kidney in renal disease. This is largely of academic interest and has little or no bearing on either of the points under discussion to-day. In spite of the activity that has so frequently been exhibited in endeavouring to elucidate this aspect of the problem of renal disease, it is still impossible to forecast the exact histological condition that will be found *post mortem* in any case of chronic nephritis. In reality the pathological findings are of little clinical importance, for what we have to deal with is not dead histology but living function. It matters little what the microscopic or macroscopic appearances of the organ may be, for, whatever the nature of the *post-mortem* changes ultimately found, they all operate during life in one direction, and give rise to a more or less impaired efficiency of the renal system with all its detrimental consequences.

Looking at the problem from the biochemical point of view, I think all observers are now generally agreed that two distinct types of chronic renal disease are encountered. In the first type to be described the chief symptom is marked oedema, and frequently no other important manifestation is present. The accumulation of fluid in the system is often so great that the internal organs of the chest and abdomen are waterlogged, and unless relief is afforded the patient dies from what may be described as drowning. Sometimes a certain degree of cardiac and general weakness is also present, and the patient may occasionally succumb from cardiac failure and general asthenia.

The Hydraemic Type of Nephritis.

On investigating such a case by the usual biochemical tests no evidence of renal inefficiency is found, with the exception that chlorides are either absent or deficient. The amount of urine passed is small, and it always contains excessive amounts of protein, and frequently large numbers of hyaline and other casts, but there is little or no evidence of cardio-vascular changes. Examination of the blood shows no retention of nitrogenous bodies; the percentage of urea and other nitrogenous urinary constituents is normal, or even above the average, and the urea concentration test shows that the kidney is capable of concentrating urea nearly if not quite as well as in the normal subject. Shortly, in such a case there is no evidence whatever of any defect on the part of the renal system in eliminating the waste products of nitrogenous metabolism; the only apparent failure is in the excretion of salt and water. Because of the marked retention of water in these patients I have on former occasions referred to this type of case as the hydraemic variety of chronic nephritis; in a general way the condition corresponds to the textbook description of chronic parenchymatous nephritis, but it is really more a subacute than a chronic condition, for in a comparatively short time either the oedema clears up or the patient succumbs.

The Azotaemic Type of Chronic Nephritis.

This type of chronic nephritis is quite different in its manifestations from the hydraemic variety just described, and is characterized by a defect on the part of the renal tissue in the elimination of nitrogenous waste products. Salt and water are excreted quite well; indeed, the amount of urine passed is often excessive. In typical advanced cases, examination of the blood shows an increase in the urea and other nitrogenous bodies such as uric acid and creatinin. The normal power of the kidney to secrete a urine containing a much higher concentration of urea and other bodies than exists in the blood plasma is markedly interfered with, so that instead of concentrating urea in the urine to an extent 70 to 100 times that present in the blood the concentration is much lower and the urine may not contain more than 10 times or less the urea in the blood. The urea concentration test gives low figures, and frequently the diastatic value is also low. This condition is often associated with cardio-vascular changes, which may be very marked. Generally, albuminuria is not very extensive; indeed no protein at all may be passed. Large numbers of casts are often present, but, on the other hand, it may be impossible to detect any casts even in carefully centrifuged specimens. Since the principal result of this type of chronic disease is an interference with the normal power of the kidney to excrete nitrogenous bodies, it may be referred to as the azotaemic type. This is the condition which is always present in real chronic renal disease and it corresponds with the usual textbook heading of chronic interstitial nephritis.

Mixed Types of Chronic Nephritis.

The above brief description of the two types of renal disease refers to typical cases. Not infrequently the two types may be manifest in the same patient, when marked oedema and retention of fluid will be associated with a more or less definite inability on the part of the kidney to excrete nitrogenous bodies and to concentrate urea and other substances. This combination frequently gives rise to a very grave clinical condition, and often terminates fatally.

Briefly, the chief points which characterize the different types may be summarized as follows:

Hydraemic Type.	*Azotaemic Type.*	*Mixed Type.*
Marked retention of fluid in tissues; severe oedema, etc.	No oedema.	Oedema may be well marked.
No retention of nitrogenous products.	Tendency to retention of nitrogenous products.	Retention of nitrogenous bodies.
Retention of salt and water.	No retention of salt and water.	Retention of salt and water.
Little evidence of cardio-vascular changes.	Cardio-vascular changes tend to be well marked.	Cardio-vascular changes may be marked.

Indications on which Prognosis is Based.

The prognosis in any case of chronic nephritis depends chiefly on three factors: (1) the general clinical condition of the patient; (2) the physical state of the cardio-vascular system; (3) the results of biochemical tests.

With regard to the clinical condition it is unnecessary to say much here, since the main symptoms of chronic nephritis are well recognized. General weakness, loss of flesh, severe headaches, vomiting and gastro-intestinal symptoms, twitching of the muscles, convulsions, mental phenomena, and other uraemic manifestations are, if at all well pronounced, sure evidence of a grave condition which indicates a bad prognosis. It is, of course, well understood that even very definite uraemic manifestations—such as convulsions, for instance—are

not necessarily associated with an immediately fatal issue, and sometimes patients recover temporarily and live for several months, or perhaps a year or more, after these attacks. In my experience, however, no patients in whom the above symptoms were well pronounced lived for any considerable time. Further, in all cases the prognosis is markedly influenced by the state of the cardio-vascular system. This will be fully discussed later.

With regard to renal tests it may at once be said that they afford much more definite evidence of the real state of affairs than is indicated by the clinical condition. Indeed, it is not uncommon to have patients bordering on fatal uraemia who show practically no clinical symptoms whatever, and who are quite unaware that they are suffering from any serious disease. Such patients always show quite definite evidence of the true condition when subjected to renal tests. So marked is the contrast between the clinical condition and the results of tests in some patients that at first one hesitated to accept the grave indications of the tests. Unfortunately, however, in the great majority of cases the result belied the clinical condition, and very soon definite symptoms appeared, terminating in the death of the patient. As the result of observing a large number of patients suffering from nephritis I now take the view that in cases where the clinical condition is not in accordance with the results of tests the clinical condition should not be considered very seriously. I am aware that this view is not accepted by all observers, but on inquiry it will generally be found that the upholders of the clinical condition as against the results of renal tests are generally individuals who have had little or no personal experience of modern methods of renal investigation.

Methods of Examination for Renal Efficiency.

Whatever tests an observer makes use of, it is important that he should adopt some definite system and apply this in all cases. This is the only means by which familiarity with the results of renal tests can be obtained, and by no other method is it possible to arrive at a correct interpretation of these results. At St. Thomas's Hospital we make use of the following scheme; it is easily carried out, and, in my opinion, furnishes all the information required in the great majority of renal patients. In each subject the following points are investigated:

A. General condition and symptoms.
B. Cardio-vascular condition: Blood pressure; position of apex beat; nature of second aortic sound; condition of peripheral arteries.
C. Renal tests: (1) Blood urea estimation. (2) Examination of urine for protein, casts, blood, leucocytes, etc. (3) Urea concentration factor. (4) Urea concentration test. (5) Diastatic test.*

The Part Played by Renal Tests in Prognosis.

Before proceeding to a discussion of the importance of the cardio-vascular condition in prognosis, it will simplify matters if the interpretation of the renal tests referred to is now described. In chronic renal disease the results of blood examination, taken in conjunction with the urea concentration test, furnish perhaps the most useful knowledge as to the condition present.

Examination of the Blood.

The estimation of the so called non-protein nitrogen of the blood is of very great value, but since the blood urea is more easily estimated than the total nitrogenous products the content of the blood in urea is frequently relied on in renal investigations. This estimation gives, in the great majority of cases, all the information required, but it must be understood that the normal variations of blood urea are comparatively large and depend to a great extent on the nature of the food. In the healthy normal individual on ordinary diet the figure for blood urea should lie somewhere in the region of from 20 to 40 mg. per 100 c.cm. blood. In elderly people, however, it is not uncommon to find 50 mg. or even more, without any definite evidence of renal disease apart from the normal senile changes. While one might be justified in taking a serious view in the case of a young patient, aged say 20 years, whose blood contained 60 mg. urea per 100 c.cm., a similar urea content in a patient of 75 years, and taking a similar diet, would have an entirely different significance. It is impossible to give exact figures, since the blood urea content varies so much as the result of different factors; but in general it may be said that the older the patient the more liable he is to have an increased blood urea content, and for practical purposes the blood urea concentration of the average normal individual on ordinary diet may be taken as ranging from about 15 mg. per 100 c.cm. in the young adult to 60 mg. or so in individuals over 70 years of age. When we get beyond this amount, the condition is undoubtedly abnormal, but any conclusions drawn from blood urea examinations must be considered in relation to age and diet. A persistent high urea content of over 60 mg. per 100 c.cm. in a young man, or a somewhat higher content in an elderly man, is of grave significance, as it indicates that probably about three-quarters of the renal tissue is not functioning.

It is most important to note that no prognostic significance can be attached to a single blood urea estimation, unless other tests and the clinical symptoms present indicate that the condition is really a chronic one, for temporary increases of the blood urea are by no means uncommon in patients suffering from very slight degrees of nephritis, and even in cardiac and other cases where there is no reason to suspect the presence of nephritis at all. Persistent high blood urea, however, is a most important feature, and is of much significance in enabling us to form an opinion as to the gravity of the condition. In chronic diseases the increased urea is practically always accompanied by some increase in the uric acid and creatinin of the blood as well, and when these substances are found to be definitely raised the outlook is certainly bad. An increase of blood urea, without a corresponding increase in the total non-protein nitrogen, is not necessarily of much importance, but it is rarely, if ever, that a definite increase in urea concentration is found in chronic nephritis without a corresponding increase in the uric acid and creatinin. In certain non-renal conditions this may occur, but even then it is unnecessary to estimate anything but the urea, for the true aspect of the case can be ascertained by combining the result of this test with that found by means of the urea concentration factor and the urea concentration test now to be described.

Urea Concentration Factor.

One of the chief functions of the kidney is to excrete the waste products of the blood in a concentrated form in the urine. A normal kidney has to deal, on the one side, with blood containing, say, 20 mg. urea per 100 c.cm.; while, on the other side, it secretes a urine containing perhaps 1,600 mg. urea per 100 c.cm. Thus in the formation of urine it concentrates the blood urea 80 times, and it is this power of concentrating that is referred to as the urea concentration factor. In disease this power of concentration is frequently very much diminished, the extent depending, of course, on the gravity of the lesion. In chronic nephritis of moderate severity the urea concentration factor may amount only to 30 or 40, while in severe cases it may be as low as 5 or even lower. Generally speaking, when this factor is below 10 the outlook is grave. The urea concentration factor should always be estimated in patients in whom a blood urea estimation is made by taking a sample of urine immediately after taking the blood and estimating the urea in both blood and urine. The result obtained from the fraction

$$\frac{\text{Milligrams of urea in urine per 100 c.cm.}}{\text{Milligrams of urea in blood per 100 c.cm.}}$$

gives the urea concentration factor.

This factor is of very great value in correcting our interpretation of certain cases in which the blood urea is high. If the urea concentration factor is also fairly high—or, in other words, if the urine contains a high percentage of urea (say 2.5 or so)—it is very improbable that the kidneys are inefficient, and the high blood urea is probably dependent on some accidental condition rather than on renal changes.

Urea Concentration Test.

This test was introduced by Maclean and de Wesselow a few years ago, and is based on the principle of ascertaining the power of the kidney to concentrate urea in the urine when an excessive supply is present in the blood. The patient, after emptying his bladder, receives 15 grams urea dissolved in a few ounces of water. Urine is collected at the end of each hour for two or three hours and the urea content estimated. Generally the urine passed at the end of the second hour shows a higher concentration than that of the first hour, and this sample is usually taken for the urea estimation. The lower urea content of the first hour's urine is due to diuresis set up by the urea; this diuresis generally passes over during the first hour, but may continue so as to

*For a full description of these tests see *Modern Methods in the Diagnosis and Treatment of Renal Disease.* Constable and Co., London.

influence the result of the second hour's urine. In such cases the urine passed after the third hour should be taken. The total amount of urine excreted should not exceed 120 c.cm. during the hour in which the urine taken for the urea estimation is passed. It is important to note that this test depends on concentration of urea alone and not on the amount of urea passed during a given period or other irrelevant points. It is necessary to emphasize this, as the principle of the test has been completely misunderstood and mixed up with other tests in quarters where, perhaps, such confusion might hardly be expected to prevail.

If after the ingestion of 15 grams urea the patient passes a sample of urine containing over 2 per cent. urea, the renal condition is fairly good; if the concentration is 2.5 per cent. or over, experience indicates that the kidney may be accepted as being quite efficient. In the absence of diuresis, concentrations of 1.5 per cent. or so indicate a moderately severe condition, but where the concentration is only 1 per cent. or less the outlook is grave.

Diastatic Test.

This test has been much utilized in the investigation of renal disease, but its results are somewhat erratic and its interpretation frequently difficult. The test depends on the fact that normally a certain amount of diastase is secreted from the blood into the urine, the amount passed being dependent on the integrity of the kidney. Expressed quite empirically, the urine of a normal individual generally contains from 6 to 20 units of diastase. When the kidneys are diseased the amount of diastase in the urine is reduced, and may be represented by a value of 1 or even less. In short, the lower the diastatic value the more intense the pathological changes in the kidney are likely to be. The test is useful but too erratic to be of much value by itself; in conjunction with other tests it is sometimes helpful.

In the absence of marked cardio-vascular lesions the interpretation of these tests and their bearing on prognosis may be summarized as follows. When severe cardio-vascular manifestations are present in addition to the nephritis the prognosis is correspondingly worse.

Blood Examination.

When the blood urea is persistently much over 50 milligrams per 100 c.cm. in a young adult, or 60 milligrams in an elderly subject, the prognosis is not hopeful, provided the other tests give similar indications. The possibility of increased blood urea as the result of a temporary exacerbation grafted on to a chronic nephritis must not be lost sight of, and various other causes of increased blood urea, quite apart from kidney lesions, must be remembered. In cases of high urea content there is generally an increase in inorganic blood phosphates, and such a combination is of serious import. Indeed, it would seem that the retention of phosphates is in some way connected with the onset of uraemia, so that phosphate retention must be considered as a serious indication. Progressive increase of blood urea concentration is also a most unfavourable omen.

Urea Concentration Factor.

When this is low the outlook is very grave. When it gets to the region of 2 or 3 the case is hopeless and life cannot be long sustained. Whatever the concentration of the blood urea the prognosis is good if the urea percentage in the urine is high.

Urea Concentration Test.

When the blood urea is high it is unnecessary to do this test as sufficient urea is already present in the blood, and all that is required is to estimate the urea concentration in a specimen of urine. Even if 15 grams urea be given in such a case no increase in urinary urea is obtained. When the blood urea is normal the pathological condition is naturally less severe, but the extent of the lesion can generally be indicated by the results of this test. If the urea percentage when using this test is over 2 or 2.5 the kidneys are quite efficient to carry out their functions. If much lower prognosis is more serious.

Diastatic Test.

In severe renal lesions the diastatic value will probably be less than 5, but little importance can be attached to this test alone in any given case.

Importance of Cardio-vascular Condition in Prognosis.

The state of the heart and arteries is of very great importance in helping us to forecast the probable course of chronic nephritis of the ordinary azotaemic variety. The opinion is widely held at present that arterial sclerosis and other vascular manifestations are generally associated with marked deficiency of the kidney, and that many of the symptoms exhibited by patients with high blood pressure are largely dependent on the renal condition. Thus it is generally assumed that a patient who shows definite cardio-vascular changes combined with slight albuminuria, and perhaps the passage of a few casts, is almost necessarily suffering from more or less grave nephritis; indeed, the tendency is to regard the cardio-vascular changes as essentially secondary to the kidney lesion. This undoubtedly is the correct view to take in many cases, but there is now sufficient evidence to prove quite conclusively that in many patients with high blood pressure and other cardio-vascular changes the kidneys may be but slightly if at all affected. The more one investigates these cases the more apparent does it become that there is no necessarily close relationship, in all cases, between the condition of the kidney and the condition of the cardio-vascular system. In many patients suffering from chronic nephritis the cardio-vascular changes undoubtedly become more marked as the renal defect progresses; there are, however, many subjects who show but little evidence of marked cardio-vascular changes, but in whom the renal system is hopelessly inefficient. Conversely, it is not uncommon to find patients with very marked cardio-vascular changes in whom but little evidence of renal disease can be ascertained. These points must always be taken into consideration in estimating prognosis, for, in a general way, apart from such accidents as cerebral haemorrhage, the outlook in a patient with high blood pressure is not so bad if the kidneys are efficient. Indeed, such patients may enjoy comparatively good health for many years, even with a blood pressure as high as 200 mm. mercury or even more. This observation explains the curious cases one occasionally finds quoted in the literature, in which a history of high blood pressure of 250 or over, frequently associated with retinitis and other eye changes, was not incompatible with the enjoyment of fairly good health for several years. In such patients the kidneys were undoubtedly effective, at least during the earlier stages of the condition; in some instances the so-called uraemic manifestations which were said to be the cause of death were nothing more than the

TABLE I.—*Patients with High Blood Pressure but Efficient Kidneys.*

No.	Date of Examination.	Duration of Disease.	Blood Pressure (Systolic).	Blood Urea per 100 c.cm.	Urea Concentration Test.	D. Value.	Protein.	Casts.
				Mg.				
1	12.4.20	5 yrs.	182	28	3.2	10	Slight	Few hyalo-granular.
	27.4.21	—	176	25	3.2	10	Trace	
	3.5.22	—	164	30	3.2	20	Slight	
2	26.3.20	5 yrs.	165	30	3.1	10	Trace	Nil.
	25.4.21	—	165	25	2.9	6	Trace	Few hyaline.
	20.2.22	—	180	22	2.8	15	Trace	Few hyaline.
3	5.9.20	4 yrs.	190	33	2.5	6	++	Few granular and epithelial.
	22.2.21	—	185	27	2.7	10	++	
	4.8.22	—	190	26	2.6	5	++	
4	12.7.21	6 yrs.	205	—	3.4	6	++	Few hyaline.
	18.4.22	—	210	24	3.1	10	++	Fair number hyaline and granular.
5	14.4.20	6 yrs.	180	33	3.0	10	Trace	Nil.
	15.5.21	—	180	29	3.1	10	Nil	Nil.
	9.4.22	—	180	—	2.9	6	Trace	Nil.
6	19.6.20	4 yrs.	180	35	2.8	15	Trace	Nil.
	6.6.21	—	195	—	2.7	15	Nil	Few hyaline.
	20.4.22	—	200	—	2.7	10	Fair amount	Nil.
7	6.6.21	5 yrs.	190	—	3.2	6	Trace	Few hyaline.
8	20.4.22	5 yrs.	210	25	2.8	6	Trace	Few hyaline.
9	14.2.22	6 yrs.	215	32	2.6	6	Trace	Numerous hyaline and epithelial.
10	20.1.22	Uncertain	240	26	3.1	10	Fair amount	Few hyaline.
11	15.3.22	5 yrs.	210	—	2.5	10	Trace	Numerous hyaline and epithelial.
12	20.12.21	4 yrs.	206	35	3.3	10	Trace	Nil.
13	10.2.22	5 yrs.	193	—	3.0	15	++	Few hyaline and epithelial.
14	6.2.22	Uncertain	230	24	2.9	10	Trace	Few hyaline.
15	20.6.22	21 yrs.	205	—	3.1	10	Faint trace	Few hyaline.

direct results of cardio-vascular degeneration and could not be regarded as evidence of death from renal disease. High blood pressure, when associated with definite and advanced renal changes, may be regarded as hopeless. In Table I are given the results obtained in a series of 15 patients with high blood pressure and vascular changes, in whom renal efficiency tests showed definitely that the kidneys were but little affected and quite efficient to perform their ordinary functions. In the majority of these patients there was a history of acute nephritis some years before. In spite of the high blood pressure and other changes present, the prognosis in such cases is much more hopeful than it would be if the renal system were badly involved.

That there are some grave cases of nephritis in which the cardio-vascular system is not involved to any appreciable extent is seen from the results given in Table II. Here, as the figures show, the renal efficiency in many cases was hopelessly bad and the prognosis about as grave as could be.

TABLE II.—*Patients with very Defective Kidneys, but no Blood-Pressure Changes.*

No.	Duration of Disease.	Blood Pressure.	Condition of Arteries.	Blood Urea per 100 c.cm.	Urea Concentration Test.	D. Value.	Condition of Urine.
				Mg.			
1	6 yrs.	160	Good	194	0.85	1	Large numbers of hyaline, granular, and epithelial casts. Much protein.
2	4 yrs.	150	Good	200	0.9	1	Casts of all kinds exceedingly numerous. Much protein.
3	Uncertain	125	Good	240	0.9	2	Protein and casts in abundance. Some leucocytes.
4	Uncertain	145	Fair	303	0.7	—	Fair amount protein. Hyaline and epithelial casts.

Note.—The position of the apex beat was normal in Cases 1, 3, and 4; in Case 2 it was just inside the nipple line in the fifth space. The second aortic sound was normal in all four cases.

It is no doubt true that slight renal involvement associated with marked cardio-vascular changes is not more common than the converse—marked renal involvement with little or no cardio-vascular changes. Usually, of course, chronic nephritis is accompanied by some involvement of the cardio-vascular system, but this is not necessarily very marked, and varies considerably in extent. Types of marked involvement of both cardio-vascular and renal systems are given in Table III.

TABLE III.—*Patients showing Well-marked Vascular and Renal Lesions.*

No.	Date of Examination.	Duration of Illness.	Blood Pressure.	Blood Urea per 100 c.cm.	Urea Concentration Test.	D. Value.	Condition of Urine.
				Mg.			
1	2.9.21	12 yrs.	208	—	1.1	1	Much protein; numerous casts of all kinds.
2	5.12.21	7 yrs.	184	—	1.3	5	Fair amount of protein; many epithelial casts.
3	6.8.21	6 yrs.	178	60	1.1	6	Very large amount of protein; numerous casts.
4*	7.7.22	4 yrs.	280	—	0.9	2	Protein in fair amount. Numerous epithelial and granular casts.
5	8.4.22	5 yrs.	258	—	1.0	4	Very large amount of protein with very numerous casts.
6	6.4.22	6 yrs.	250	95	1.2	4	Protein moderate; epithelial and hyaline casts.
7*	10.10.21	Uncertain	246	210	0.7	1	Fair amount of protein; very many casts of all kinds.
8*	29.5.21	7 yrs.	230	—	0.6	2	Much protein; fair number of epithelial and granular casts.
9	31.3.22	11 yrs.	200	—	1.0	1	Protein abundant; fair number of casts.
10*	7.10.21	Uncertain	280	92	1.2	5	Moderate amount of protein; few epithelial casts.

* These patients died.

Some General Observations.

In the majority of renal patients suffering from chronic interstitial nephritis (azotaemic nephritis) it is not very difficult to arrive at a fairly accurate prognosis when the method of examination suggested is carried out; this is more especially the case when the patient is under observation for some time. In severe conditions the clinical symptoms alone will often indicate that the end cannot be far distant. Probably it is true that chronic renal patients with marked eye changes, such as retinitis and haemorrhage, do not as a rule live more than one or two years, but there certainly are many exceptions. When, however, we consider very carefully the state of the cardio-vascular system and the results of renal tests, there is very seldom any great difficulty in arriving at a definite conclusion as to the condition existing at the time of examination. On the other hand, it is not so easy, in some cases, to estimate the probable rate of progress of the disease, and frequently this can only be done by repeated examinations at intervals. Again, the liability of contracting an acute attack of nephritis must always be considered, but cannot of course be foreseen, and to this extent we must always be working in the dark.

The following results (Table IV) obtained from patients with varying degrees of nephritis illustrate some of these points:

TABLE IV.

No.	Blood Pressure (Systolic).	Blood Urea per 100 c.cm.	Urea Concentration Factor.	Urea Concentration Test.	Condition of Urine.	Opinion of Case.
		Mg.				
1	240	110	8	0.9	Much protein; epithelial and granular casts.	Condition serious; prognosis very bad.
2	200	38	60	3.1	Protein small amount; few epithelial casts.	Kidneys good; prognosis good as regards renal condition.
3	160	30	50	2.8	Fair amount of protein; few hyaline casts.	Condition fairly good; prognosis quite hopeful.

Note.—The arteries were thickened in Case 1, and slightly so in Case 2; in Case 3 they were normal. In Case 1 the apex beat was in the left nipple line, fifth space; in Cases 2 and 3 it was in the normal position.

Prognosis in Surgical Operations.

Not infrequently the question of operation arises in the case of patients who happen to be suffering from some degree of chronic nephritis. In all such patients renal tests on the lines just indicated should be carried out, when it will generally be quite possible to say whether or not the renal lesion precludes operative interference. If there is no increased blood urea, and the result of the urea concentration test is good, it may be stated with some certainty that the renal condition does not contraindicate operation. This is a very large subject which it is impossible to discuss more fully here, but it may be said that experience shows that extraordinarily accurate forecasts can be made.

Frequently after operations on the genito-urinary organs, or after other major abdominal operations, the patient does very well for a few days, and then passes into a condition which is frequently associated with serious symptoms, and is variously labelled as "peritonitis," "acute post-anaesthetic dilatation of the stomach," "delayed shock," "paralysis of the intestine," etc. It is hardly recognized that the majority of these cases appear to be of a uraemic nature, and generally clear up if the kidneys are moderately efficient. In conjunction with Dr. I. Jones I have made a considerable number of observations on this type of case, but as a full report will shortly appear it is unnecessary to discuss the matter further at this stage.

Treatment of Chronic Nephritis.

The detailed treatment of chronic nephritis requires little comment; it really resolves itself into the treatment of symptoms and is carried out by the use of the ordinary well-known remedies, with slight variations depending on the particular fancy of the medical practitioner. In all cases the general régime is important. Warm clothing, hot baths, careful attention to the bowels, avoidance of exposure to cold and wet, and, if possible, residence in a warm climate, are factors which no doubt frequently result in prolonging life. Unfortunately, it is often difficult or impossible for the patient to avail himself of all these measures. When he can do so nobody will, I think, deny that they are likely to prove helpful. The chief interest, however, in the treatment of chronic renal disease revolves round the question of diet, and nearly all medical men are careful to give very stringent injunctions as to the nature and amount of the

food which the nephritic patient may eat. In discussing this problem it is necessary to remember that the two forms of disease already mentioned—the hydraemic or chronic parenchymatous form and the azotaemic or chronic interstitial form—present rather different problems, and must be dealt with separately.

Diet in Chronic Interstitial or Azotaemic Type.

The usually accepted diet for chronic interstitial nephritis is one in which the protein constituent is low. The view adopted is that, the renal system being the chief means by which waste nitrogenous products are eliminated, these products should be reduced to the minimum in order to spare the kidneys. This conception, no doubt, contains a germ of truth, but it was formulated in other days when our conceptions of protein metabolism and of renal activity were very different from what they are to-day. Really it is quite an open question whether protein in itself is at all detrimental even in cases of advanced renal disease. I am at present carrying out experiments in connexion with this problem, but the subject is a difficult one from the experimental standpoint. It is quite certain that even complete withdrawal of protein from the diet in cases of advanced lesions associated with uraemia does not influence the uraemic manifestations. It is frequently not difficult by the use of a carbohydrate diet to reduce the blood urea and non-protein nitrogen in a uraemic patient to well below the normal value, but this does not influence the uraemia. Until our information on this subject is largely increased it will, no doubt, be wise to restrict the amount of protein consumed when treating advanced cases. On the other hand, it is important to bear in mind that the ordinary healthy individual requires protein in order to maintain health, and that the minimum amount necessary seems to be about one gram per kilogram of body weight. When this amount is materially reduced the individual suffers sooner or later. It would, therefore, seem best to allow this amount of protein in all but advanced cases. In patients with slight or only moderately severe lesions, it seems best to give a diet containing a fair amount of protein, and the present custom of putting such patients on slops containing but a minimum of protein is to be deprecated. Many such patients suffer more from treatment than from the renal condition. When, therefore, the renal tests show that the kidney lesion is not severe, much benefit is frequently derived from an increase of protein food. On the whole, there is little doubt that the dietetic treatment of the milder forms of interstitial nephritis is at present too strict, and the patients do much better on a more liberal ration. In every case before putting a patient on any form of restricted diet the condition of the kidneys should be carefully ascertained, for sometimes the presence of a little albuminuria is the sole condition that can be found. In such patients dietetic treatment is superfluous, and frequently does harm. In the more severe types of disease it is probably advisable to limit the protein, but even here a fair amount should be given. It must be remembered that the body will itself supply waste products from its own tissues when little or no protein is given as food, so that it is impossible to eliminate altogether the work of the kidneys in excreting waste products.

Diet in Hydraemic or Parenchymatous Nephritis.

As already indicated, there is no retention of nitrogenous waste products in this variety of disease, and no apparent difficulty on the part of the renal system in excreting these products. Theoretically, therefore, there is no need to restrict protein. Since a large amount of protein is generally lost in the urine, an additional reason for the giving of protein is supplied. Practically it is found that a large protein diet is generally more effective than any other measure in clearing up the oedema and in helping to restore the patient to comparative comfort. This type of disease constitutes a phase which is essentially of moderate duration, for under favourable conditions it tends to pass into what is usually a mild form of interstitial nephritis. It may, however, pass into a very severe form of the interstitial variety, and in such cases the prognosis is grave. Until this condition—representing the chronic interstitial type of nephritis—supervenes, the ascites and oedema persist. Epstein and others have shown that the best method to get rid of the excess of tissue fluid is to give large amounts of protein in the diet. There is no doubt that large protein ingestion gives wonderful results in many cases, and this method should be adopted with all patients suffering from typical hydraemic nephritis without any azotaemia. Sometimes the elimination of salt from the diet has a marked beneficial effect, but generally this alone is not sufficient; combined with high protein diet it is very often helpful. The exact mechanism by which protein acts in clearing up the oedema is not quite understood, but the increase of blood urea which naturally follows the increased protein ration is probably the chief factor on which this favourable result depends. The urea acts as a diuretic and so causes an increased flow of urine. In proof of this it is frequently found that daily dosage with 15 to 30 grams of urea for a few weeks will clear up very obstinate cases. In short, the best treatment for hydraemic nephritis is a large salt-free protein diet, accompanied at first with some urea given by mouth. This should be combined with rest in bed, hot-air baths, and free action of the bowels.

Decapsulation of Kidneys in Hydraemic Nephritis.

This is the type of case in which decapsulation of the kidneys is frequently attended with an improvement of the condition. While the results of this treatment are by no means uniform, it does seem that many patients suffering from obstinate hydraemic nephritis are greatly benefited by this procedure. The symptoms appear to suggest that the renal channels are blocked up with débris and swollen cells so that fluid can pass with difficulty, and so it is easy to understand how relief of this tension might give good results. Personally I have not had much experience of this treatment, but what I have seen suggests that in hydraemic nephritis operative procedures of this nature will play a much larger part in the future than has been the case in the past.

Though the discussion of the treatment of chronic nephritis is necessarily somewhat curtailed, we must face the fact that at present there is no specific treatment for this condition, and much work must still be done before we can be at all certain of the best means of combating this insidious lesion, and, if possible, preventing its advance.

DISCUSSION.

Dr. JOHN D. COMRIE (Edinburgh) said: One should not lose sight entirely, I think, of certain old and simple methods of testing the condition of the kidneys. The absolute amount of albumin that a nephritic patient passes is no criterion whatever of the state of kidney inefficiency, for the leak may be of a merely functional character, even when it is pronounced in degree; and on the other hand the kidneys are often very much damaged in structure and in efficiency when a mere trace of albumin appears in the urine. Nevertheless, if a case of parenchymatous nephritis be under continual observation and treatment, and if the albumin be carefully estimated every day, a useful indication as to prognosis is obtained, so that if a progressive diminution is noted the sign, *caeteris paribus*, is favourable. Again, the question as to how the patient secretes water—or in other words the maintenance of the normal proportion between the amounts of day urine and of night urine—is of much importance. This is an indication mainly, I think, of the state of the cardio-vascular system as regards hypertrophy and sclerosis. Various methods have been suggested by Leathes,[1] John,[2] etc., for carrying out this test, but the most satisfactory in my opinion is to measure the quantity of night urine (9 p.m. to 7 a.m.) in one collection, and the day urine in seven two hourly (7 a.m. to 9 p.m.) collections. Normally the total night urine is not greater than any one of the two-hourly day urine samples, which show also considerable fluctuation. In the nephritic with marked arterio-sclerosis there is "fixation" of the rate of excretion, the two-hourly excretion tending to be more and more the same by day and night as the condition becomes progressively worse. This rule, as shown by Boyd and Malcolm Smith,[3] is not, however, always true, especially in cases of severe nephritis with little arterio-sclerosis, and thus the test is not of value in all cases. The same unreliability attends the estimation of the rate of secretion of chlorides, of potassium iodide, and of some other easily soluble substances, whose amount is a function of the water excretion. The amount of pancreatic diastase excreted in the urine I have also found to be so variable as to be often unreliable.

The three tests upon which I place most reliance are: (1) the estimation of blood urea; (2) the urinary urea concentration test; (3) the excretion of phenolsulphonephthalein. Any one test is liable to have fallacies, and the kidneys may give a fair reaction with one while being less

[1] *Lancet*, 1920, ii, p. 923.
[2] *Münch. med. Wochenschr.*, February, 1921, p. 180.
[3] BRITISH MEDICAL JOURNAL, 1921, ii, p. 428.

efficient with the others, so that these tests form useful mutual controls.

1. The estimation of blood urea is simply carried out by the urease method. One must be sure that the ferment used is active, and for the same reason one must be careful not to raise the temperature of incubation above 110° F. Any rise above 50 mg. per 100 c.cm. of blood indicates a marked urea retention; and if it be permanently over 100 the case is almost invariably a serious one; in bad cases of acute uraemia it may reach two or three times that amount and death is then very likely. A negative result is not, however, proof of normal renal efficiency, since persons with marked nephritis often have a normal blood urea of 30 mg. or thereabout. This applies to cases of subacute diffuse nephritis, or hydraemic nephritis, with a special tendency to dropsy. In such cases the patient may throughout the whole course of the disease show no accumulation of urea in the blood. This fact is particularly important to bear in mind in cases where the estimation of blood urea is used as a test for the capacity of the patient to undergo a severe surgical operation. The blood urea is also a valuable dietetic indication. These dropsical patients with low blood urea are benefited by a diet containing protein foods of easy digestibility—for example, mutton, chicken, and fish—while cases of the azotaemic type, with raised blood urea, should be kept for long periods on a milk and carbohydrate diet.

2. The urinary urea concentration test is the simplest test to carry out, and affords a very good general indication of the renal efficiency. It is carried out by administering 15 grams of urea in 200 c.cm. of water, and estimating the percentage of urea in the second hour's specimen of urine. A percentage of 3.5 or over indicates a normal renal function; over 2 per cent. it is compatible with a fair degree of health; and persisting below 2 per cent. in spite of treatment it is very unsatisfactory. Persisting below 1 per cent. it is a sign of impending death. It is often noticed that the diuresis caused by the urea produces a low reading, and I would suggest a correction as follows for the watery state of the urine produced by this hydrodynamic response of the kidney. The usual amount of urine passed after the urea test, in the second hour, is about 150 c.cm., and the reading could be corrected to that amount by the following formula—

$$C = U \times \frac{Q}{150},$$

where C is the concentration expressed in terms of the average quantity of urine passed in the second hour after the test, Q the actual quantity passed, and U the percentage of urea found in this. For example, if the patient passes 250 c.cm. in the second hour and this is found to contain 2 per cent. of urea, then

$$C = 2 \times \frac{250}{150} = 3.3 \text{ per cent.},$$

that is, the figure corrected for the watery diuresis. Otherwise, if the quantity of urine is much above or below 150 c.cm., one must simply discard the test and try it again next day.

3. The phenolsulphonephthalein test has been used by the writer[1] constantly for the past twelve years, and he regards it as the best, though not the simplest, individual test. It has certain requirements and fallacies. In the first place, one must measure very accurately for intramuscular injection 1 c.cm. of the phenolsulphonephthalein solution (containing 6 mg. of pigment). The urine must be completely voided for the two-hourly samples, and rendered strongly alkaline by 10 c.cm. of 10 or 15 per cent. caustic soda. The pigment of the urine, and especially the presence of blood, constitute considerable fallacies unless care be exercised. These can be avoided by filtration and the use of a suitable optical filter introduced below the prism of the colorimeter, as shown in the following table, which gives the average of a number of observations:

	Greenish-yellow Diabetic Urine.	Dark Brown Clear Urine.	Urine Smoky from Blood.
Actual percentage of phenolsulphonephthalein present	50%	50%	50%
Reading unfiltered	59%	70%	55%
Reading when filtered and colour screen used	53%	53%	52%
Reading when shaken with charcoal and filtered	—	—	46%
Reading after shaking with lead acetate and filtering	0	0	0

[1] *Edin. Med. Journ.*, February, 1922, p. 3½.

The most correct reading is thus obtained by filtering the urine through a fine filter paper and using an optical colour screen. The excretion of this substance should take place chiefly in the first hour, and the amounts of the two hours should total at least 70 per cent.; excretion of 50 per cent. is compatible with recovery under treatment; 30 per cent. is low, but life may proceed on a low plane of vitality; an excretion below 20 per cent. is bad, and if it persists much below this figure death usually ensues within a few months.

Dr. J. ODERY SYMES (Bristol) said: I wish to confine my remarks to the prognosis and treatment in chronic parenchymatous nephritis. All textbooks agree that this is one of the most unfavourable and rapidly fatal forms of nephritis. Jeanselme in his recent work, *Maladies des Reins*, says: "Death takes place in from three to twelve months, and is often hastened by cardio-pulmonary or intestinal complications, septic infections, cachexia, and emaciation." The question I wish to ask is: Is there such a condition as pure chronic parenchymatous nephritis (large white kidney), and, if there be, is the prognosis so invariably unfavourable as is generally accepted? By chronic parenchymatous nephritis is generally meant a tubular nephritis accompanied by much oedema, deficient excretion of salt, diminished quantity of urine of high specific gravity, much albumin, numerous casts, but in which uraemia is uncommon, the blood pressure is not raised, ocular symptoms are rare, and, most important of all, the renal efficiency is fair. My clinical experience has been that if such a condition as tubular or chronic parenchymatous nephritis exists it is extremely rare, and if it exists we must considerably modify our view of the gravity of the prognosis.

Since I have adopted renal efficiency tests and blood urea estimations I have had fifty-two cases of nephritis in my wards. Two of these were diagnosed as chronic parenchymatous nephritis. Both are still alive three years from the commencement of their illnesses, and a closer examination of their cases makes it almost certain that the condition was one of subacute diffuse nephritis. Similarly with cases seen before the renal tests were introduced—a very striking example of chronic parenchymatous nephritis who was admitted under my care in 1904 is still alive to-day. He was in the Bristol General Hospital from February to October, 1904, with gross oedema requiring repeated tapping, and was discharged in the same condition. He had all the typical signs—anaemia, dyspepsia, small amount of urine (specific gravity 1020), albumin 7 to 9 parts per 1000, low blood pressure, urea excretion fair. The oedema persisted for six months after his discharge. In 1911 the high total of daily urine, low specific gravity, and a trace of albumin suggested secondary sclerotic changes, and in 1919 this was the same, and his phenolsuphonephthalein excretion was 23 per cent. only. The blood nitrogen was very high. The sodium chloride excretion was normal, the two hourly specific gravity never above 1012. Here was a case—the most typical of chronic parenchymatous nephritis I can produce in twenty years of hospital work: yet he has lived eighteen years after his initial attack. I recall one other case, a minister. He was superannuated in 1885 on account of chronic parenchymatous nephritis (large white kidney), but is alive and well to-day at the age of 69 years. The albumin amounts to 2 parts per 1000, the vessels are slightly thickened, the heart is not enlarged, the blood pressure not raised. The point I wish to emphasize is that we must either sternly modify our conception as to the grave prognosis in this disease, or we must deny altogether that there is such a condition as a chronic tubular nephritis. Personally, I favour the latter course not only on clinical but also on pathological grounds, for, except in the kidney of pregnancy, I never see a case in which the brunt of the disease is borne by the tubuli whilst the glomeruli are but slightly affected. Nephritis is essentially a vascular intoxication, and invariably the glomerulus suffers primarily and the tubular destruction is entirely secondary and consequential. There is no ground for the view that large white kidney is a disease *per se* and that the prognosis is peculiarly unfavourable. The terms "parenchymatous nephritis" and "tubular nephritis," with their evil omen, ought to be abolished from our nomenclature, and the large white kidney regarded as a phase of a glomerular (or diffuse) nephritis; a subacute or chronic phase, probably progressive towards an interstitial nephritis but not necessarily immediately dangerous, and indeed compatible with a prolonged period of comfortable living.

With regard to the question of treatment of the chronic oedematous type of nephritis I have only to note two points.

First, it is not worth while submitting the patient to the prolonged salt-free diet of Karrell or the still more prolonged super-protein diet of Epstein when a diuresis immediate and in every way satisfactory can be established by the administration of urea. There appear to be no ill effects following the administration of urea. I have recently had two boys under my care aged 12 and 14, and one took 18,000 grains in thirty days and the other 7,000 grains in thirteen days with great benefit. The blood urea in the first case at the end of the course was 50 mg. per 100 c.cm. For many days after the drug is withdrawn the diuresis continues and the oedema shows no sign of returning. I have not hesitated to give to these oedematous cases a diet containing 30 to 50 grams of protein a day, and they appear to do better than when on a limited scale. The second point is that the oedematous case may be kept too long in bed. There is no doubt in my mind that a moderate degree of exercise hastens the disappearance of the oedema and generally benefits the patient. It should not be forgotten that chronic nephritis in any form leads to an anaemia of the aplastic type, and that this condition is greatly benefited by the administration of iron and arsenic.

Professor J. SHAW DUNN (Birmingham) said: Until we have more certain information regarding the normal physiology of renal secretion it will be impossible to obtain any complete conception of the relation between the morbid changes in the kidneys and the impairment of renal function in nephritis. Still, something may be gained for the prognosis and treatment of chronic renal disease by a more thorough correlation of modern clinical and pathological methods of investigation. Generally speaking, in nephritis the glomeruli and tubules are always both affected by pathological change, although the type of lesion, its extent, and the proportion between glomerular and tubular lesions vary greatly in different instances. As regards type, the lesions may be grouped provisionally under the headings (1) alterative and (2) destructive.

1. *Alterative.*—Here the glomeruli are free from gross changes and their capillaries are patent: there may be some fatty degeneration of the capillary endothelium, and there is evidence that the capillary walls allow the leakage of albumin from the blood. The tubular changes are more obvious, comprising fatty degeneration, hyaline-droplet degeneration, and oedematous swelling of the epithelium, but there is often little actual catarrh or loss of cells. Where alterative changes are present in the purest form the nephritis is most purely of hydraemic type and shows least evidence of urea retention. The evidence suggests a loss of balance, a pathological modification of excretion, rather than a diminution of excretory power. It is quite possible that the function of the tubular epithelium is so altered as to cause a greater reabsorption of constituents than normal, thus accounting for abnormal retention of water and salts.

2. *Destructive.*—Here the glomeruli are obviously grossly diseased; the capillaries are often blocked by endothelial cells, or there may be closure of groups of capillaries by miliary thrombi resulting in infarction and fibrosis of the tufts. Accompanying this there may be catarrh of the glomerular epithelium, adhesions between tuft and capsule, and thickening of Bowman's capsule. All of these phenomena tend to the ablation of glomerular function, thus cutting off the function of excretion at its source. It is important that these lesions are often focal in character, and some tufts may remain normal. The tubules here also suffer markedly; the epithelium becomes lowered in type; there is much catarrh, and in later stages there is more and more total destruction and atrophy of tubules. Associated with these grosser changes in the parenchymatous elements there is extensive overgrowth of interstitial fibrous tissue. The effects of the destructive type of change are seen in purest form in so-called chronic interstitial nephritis, and comprise mainly a tendency to retention of urea and to elevation of arterial blood pressure. These effects may be assumed to depend on lack of filtration owing to loss of glomeruli. The tubular function must also be greatly diminished, as the loss of tubules is enormous; possibly this accounts for the tendency to polyuria in such cases owing to inefficient reabsorption of the glomerular filtrate. While it is possible to define these two main groups of renal lesions it is probably comparatively seldom that they occur in approximately pure form. In many instances they are combined, and, further, they occur together in varying proportion, so that it is extremely difficult, if not impossible, to project the nature of renal lesions from a consideration of the clinical aspects of a case. Reference has been made to the recognition of cases showing clinically a high blood pressure with totally unimpaired renal function. In relation to this it may be remarked that in *post-mortem* work it is much commoner to find evidences of the existence of a high blood pressure associated with arterio-sclerotic atrophy of the kidneys than with any form of chronic nephritis.

Dr. KATHERINE O. ROBERTSON (Glasgow) said: Judging from the literature on renal disease it appears that while much has been done in the study of renal disorders from the pathological, clinical, and more recently from the biochemical points of view, little attempt seems to have been made to correlate these findings, although various authorities have fully recognized this necessity. With this in view I have tried to follow my cases to the final court of appeal and correlate my clinical findings with the condition of the kidneys and blood vessels at *post-mortem* examination. So far I have only succeeded in making a complete study of six cases. These consisted of two cases of primary arterio-sclerosis with secondary involvement of the kidneys, two cases of primary chronic nephritis with secondary arterial degeneration, one case of advanced pernicious anaemia, and one case of acute malignant endocarditis. The two cases of arterio-sclerosis, Nos. 17 and 31, had many features in common. The blood pressures were respectively 190 and 240. Case No. 17, however, did not come under observation until cardiac failure had set in. Both cases complained of long-standing gastric and intestinal disturbances, and more recently of polyuria and breathlessness. Both cases had enlarged hearts. Neither case gave any history of long-standing renal disorder. Case No. 17 had been treated eleven years ago for haemorrhage from the bowel, and at that time was diagnosed as a case of cirrhosis of the liver; the heart was somewhat enlarged, but there was no albumin in the urine. Patient improved under treatment, and his health remained fairly good till three months before his death, when breathlessness and heart failure set in. By the time the patient was admitted to the hospital he was suffering from headache and the chronic slight uraemia so common in these cases. At *post-mortem* examination there was no sign of cirrhosis of the liver. Case No. 31, on the other hand, remained mentally clear almost to the end, though headache was a distressing symptom. An interesting point in this case is that about five weeks before her death a urea concentration test was carried out, and the highest point reached was 2.1 per cent. in the third hour after the usual dose of 15 grams urea by the mouth. The blood urea was estimated in the third hour and found to be 112 mg. per 100 c.cm., giving a urea concentration factor of 18. Eight days later the test was repeated, and this time the highest point reached was 1.5 per cent. in the first hour, the concentration in the third hour being 1.3 per cent.; the blood urea in the third hour was 103 mg. per 100 c.cm., giving a urea concentration factor of 12. This low reading may have been due to the fact that the patient vomited about half an hour after taking the urea, but a blood urea of 103 mg. should have stimulated a reasonably active kidney to concentrate to its fullest capacity. In cases giving good concentrations in the urine I have found that the blood urea estimated in the third hour after the dose of urea was well below 100 mg. per 100 c.cm. *Post-mortem* examination showed even more resemblance between these two cases. Both cases had hypertrophied hearts; the kidneys were granular but not much altered in size. Microscopically the vessels of the mesentery, both large and small, were greatly sclerosed and the lumen of the vessels decidedly narrowed by the multiplication of the internal elastic lamina. The kidneys showed marked interstitial and glomerular fibrosis of vascular distribution. The small vessels of the kidney were tortuous and thick-walled, in many the lumen was almost completely occluded. It seems wrong to class these as cases of kidney disease. The renal manifestation was a late symptom of the general vascular degeneration, which in each case had given rise to gastric and intestinal symptoms long before any functional change was noticed in the kidney. On the other hand we have cases Nos. 15 and 20, which were both primary kidney conditions. Here the history revealed repeated attacks of nephritis. The blood pressures were respectively 190 and 220. Case No. 15, however, was suffering from heart failure when the blood pressure was taken. They showed the headache and slight chronic uraemia of the previous two cases. Both gave a poor urea concentration and the blood urea estimated in the third hour

was high, giving a low area concentration factor. Case No. 20 showed retinal and sclerotic haemorrhages. Neither case gave a history of long-standing gastric or intestinal disturbances. At *post-mortem* examination both were found to have enlarged hearts, the kidneys were granular but not much contracted. Microscopical examination showed that the larger vessels of the mesentery and kidney were more affected than the smaller ones. The change was chiefly a medial fibrosis, though the renal artery in case No. 20 showed marked patchy thickening of the intima. The kidneys showed generalized interstitial and glomerular fibrosis. There was no sign of vascular distribution. Thus we have four cases which in the late stage were clinically indistinguishable. The albumin was not excessive; the blood pressure was high with enlarged heart; the urea concentration test was low. There was headache, restlessness, breathlessness, cardiac failure, and chronic slight uraemia tending to deepen in all four cases. The clinical difference lay solely in the history which, as has been pointed out in the arterio-sclerotic cases, centres round the alimentary tract and in the cases of chronic nephritis round the kidney. The *post-mortem* examination also showed resemblances between the four cases. The heart was hypertrophied and the kidneys were granular but of nearly normal size in all four cases. Microscopical examination showed interstitial and glomerular fibrosis in all four cases. In the arterio-sclerotic cases the fibrosis showed vascular distribution, but this was absent in the other two cases where the fibrosis was equally distributed. Another difference was seen in the distribution of the vascular degeneration which, in the arterio-sclerotic cases, affected large and small vessels alike, but in the chronic nephritis cases affected the larger vessels more than the smaller ones. This brings me to the case of pernicious anaemia, which gave a low urea concentration. It is just possible, however, that this may have been due to poor absorption, as the blood urea estimated in the third hour was very low. In this case the kidneys showed marked catarrh of the secreting tubules with cloudy swelling and some fatty degeneration. It is interesting and suggestive to note that there is one factor common to all these five cases, and that is the poor supply of oxygenated blood received by the kidney. The sixth case, one of acute malignant endocarditis, gave a very good urea concentration the day before she died. Death in this case was sudden. The kidneys showed marked catarrhal and interstitial nephritis with cloudy swelling, and were of large size. The mesenteric and renal arteries showed commencing medial degeneration. These cases all showed other interesting features clinically, biochemically, and histologically, but time does not admit of further detail.

Dr. O. L. V. DE WESSELOW (London) pointed out that, though in chronic interstitial nephritis the rise in the blood pressure often bore some relationship to the degree of impairment of nitrogenous waste products, this relationship was not one of cause and effect. In certain surgical affections of the kidney, in amyloid disease, and in cystic kidney marked nitrogenous retention was often associated with a normal blood pressure. From the point of view of immediate prognosis, he regarded the estimation of the inorganic phosphorus content of the plasma as valuable. The figure for inorganic phosphorus in the normal was in the neighbourhood of 3 mg. per 100 c.cm. of plasma. In acute nephritis figures of 5 to 7 mg. were common. An inorganic phosphorus content above 10 mg. appeared to indicate an exceedingly grave prognosis. A patient in whom a definite urea retention was associated with a retention of inorganic phosphorus was in a much graver condition than a patient showing a similar rise in the blood urea but a normal phosphorus content. From the clinical point of view the symptoms of uraemia showed a much closer connexion with phosphate retention than with retention of the nitrogenous waste products. A diminution in the calcium content of the serum was frequently found in nephritis, but this diminution did not appear to bear any relationship to the convulsive phenomena. In the only case in which he had found an extreme reduction in the serum calcium, administration of calcium per os produced no increase in the calcium of the serum. This was to be expected, since in view of the large calcium reserves of the body the deficiency in the serum was more likely to be due to a change in the chemical composition of the blood than to actual lack of calcium.

Dr. H. L. TIDY (London) thought it was our duty to correlate both the clinical symptoms of the disease and the renal efficiency tests with the histology of the kidneys. For many years physicians, from observation of clinical symptoms, had foretold with considerable accuracy the type of pathological changes which were present in the kidneys. Obviously the clinical symptoms and pathological changes had some relationship. So, too, had the clinical symptoms and the renal efficiency tests. He considered consequently that the renal efficiency tests and the histological changes in the kidneys must be capable of correlation. He did not agree with former speakers that histological types could be clearly divided into two classes, and he believed that this view was partly responsible for the failure hitherto to connect the renal efficiency tests with the histology. There were, he held, at least four types. He was surprised that the small white kidney had not been mentioned during the discussion. It was a definite pathological type which could often be diagnosed from its clinical symptoms.

Dr. E. J. TOYE (Bideford) made a few remarks on the subject from the point of view of the general practitioner. He emphasized the simplicity and utility of the urea concentration test. He concluded by stressing its great value in testing the adequacy of the renal function in cases of albuminuria of pregnancy.

Before calling on Professor Hugh Maclean to reply, the PRESIDENT emphasized the value of the urea concentration test as a means of ascertaining the actual condition and the progress of a case of nephritis. It could not replace the observation of symptoms or the study of certain other well-recognized signs, but it had the advantage, not shared by many other signs and symptoms, that the findings could be kept on record in black and white for comparison with corresponding results obtained in the same case later on. It would be a great gain if one could recognize the existence of a lesion, whether stationary or progressive, which had diminished the total functional capacity of the kidneys and yet had left them with sufficient reserve power to respond to all tests to which, at the present time, they might be subjected by the physician. Patients who came under observation on account of acute or subacute nephritis sometimes gave a history of previous attacks many years before; and one would like to know whether each of these earlier attacks had left behind it a lessened reserve of functional capacity, or whether the attacks merely revealed the weak spot in the particular patient and passed off without doing any permanent harm, and without diminishing the enormous reserve power of the kidneys.

NOTES OF A CASE OF ACUTE MYELOGENOUS LEUKAEMIA AND OF A CASE OF APLASTIC ANAEMIA.

BY

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AND

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Case of Acute Myelogenous Leukaemia.

J. S., a male aged 58, was admitted to Dr. Fleming's wards on October 28th, 1920, on the recommendation of Dr. Lang. He complained of feverish attacks, each attack lasting for one to two hours, during which his temperature rose to 104° or 105° F. and fell with profuse sweating. He had two or three of these attacks each twenty-four hours, and each commenced with a rigor. His occupation, originally that of a shale miner, had for three years been limited to loading ammonia sulphate into bags.

His past history was as follows. He had had rheumatism three months before admission, with pains in shoulders, elbows, wrists, and fingers, and the pains flitted from joint to joint. He had no fever at that time, and recovered in four weeks. There was also a history of influenza in 1919, lasting for seventeen weeks. His family history was unimportant.

On examination on October 28th, 1920, there was no splenic enlargement, no enlarged glands were found present, and nothing abnormal was noted in his blood. On November 8th the spleen was found to be definitely enlarged, and he complained of pain due to perisplenitis. His red cells numbered 3,330,000 and his leucocytes 8,000. On November 9th his leucocytes had increased to 18,500 and the differential count showed polymorphs 30 per cent., eosinophils 1 per cent., myelocytes 11 per cent., large mononuclears 13 per cent., and small lymphocytes 44 per cent. The majority of the

larger cells resembled myeloblasts, and were difficult to place accurately in any group. Films stained by Leishman's method showed a dark basophil cytoplasm in certain cells with numerous azurophil granules. Some cells had an intensely basophil-stained cytoplasm. The nuclei were large, varying in shape. Some of the cells showed mitotic division with beautiful examples of monaster and diaster stages.

On November 11th numerous petechial haemorrhages were noted over the chest, and especially round the hair follicles. On November 14th the patient died, twenty-one days after the pyrexial attacks commenced and six days after his spleen was found to be enlarged. The lymph-gland groups enlarged coincidently with the spleen, particularly in the cervical region.

[Slides of the blood, spleen, bone marrow, and liver were demonstrated.]

Case of Aplastic Anaemia.

J. W., a female aged 26, a cook, was admitted to Dr. Fleming's wards on the recommendation of Dr. John Craig, Edinburgh, on November 11th, 1920. The duration of the illness was from December, 1918, and her chief complaints were weakness and shortness of breath.

She had had no previous illness before 1918, except "headaches." Since 1918 she had a "blister-like" rash on her face, shoulders, and chest, in 1919 lasting for three weeks. There was also severe pyorrhoea, which gave continuous trouble and required much treatment. Her mother and her only sister were anaemic, and both had a history of gastric ulcer. Her father died of pulmonary tuberculosis at the age of 35.

On examination the patient was stout and very pale, but with a lemon-tinted skin. She had the usual haemic murmurs and a slightly dilated heart. There were periods of pyrexia lasting for ten days at a time with no definite periodicity. The diagnosis of aplastic anaemia was made because, during the patient's stay in the wards, extending up to the time of her death on October 19th, 1921 (a period of eleven months), her blood never showed any normoblasts or megaloblasts. There was poikilocytosis, varying in degree from time to time, but no punctate basophilia and no polychromatophilia. Anisocytosis was peculiarly marked, there being many microcytes and megalocytes.

Direct transfusion proved the only really effective treatment, although the benefit obtained was temporary.

The *post-mortem* examination showed that an extraordinary degree of haemolysis had occurred.

[Slides of the blood, the bone marrow, etc., were demonstrated.]

A CASE OF INTRAPERICARDIAL ANEURYSM OF THE AORTA.

BY

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THE patient, a labourer aged 48, attended hospital on August 10th, 1920, complaining of pain in the chest, on the right side especially, shortness of breath, and cough during the previous four weeks.

Physical Examination.

The findings at the physical examination were as follows:

A well-developed man, somewhat above the average in general physique; expression anxious, cheeks sunken, malar eminences flushed; obvious pulsation in carotid, temporal, brachial, and other superficial arteries. Chest wall well covered, normal contour except for visible pulsation to the right of the sternum in the third, fourth, and fifth spaces; area of cardiac dullness extends 4 inches to the left of the mid-sternal line to the apex beat, which is situated in the sixth intercostal space and 3½ inches to the right of the mid-line at the level of the fifth rib and corresponding space. The apex beat is forcible in character, diffuse in extent; there is a heaving impulse to the right of the sternum of maximum intensity in the fifth, but also felt in the third and fourth spaces. On auscultation a short systolic and long diastolic murmurs are audible over the entire precordium, the latter being of maximum intensity at the aortic area, but clearly heard over the dull region to the right of the sternum, and conducted upwards into the vessels at the root of the neck. The arteries are thickened and tortuous, the radial pulses collapsing in character and synchronous; the jugular veins are unduly prominent in the recumbent position, otherwise there is no evidence of venous stasis or obstruction of either superior or inferior vena cava. The pulmonary excursion and air entry are normal over both lungs, no tracheal tug; no indication of pressure on vagus, phrenic, recurrent, or sympathetic nerve trunks. The electrocardiogram suggests left ventricular preponderance, but is otherwise normal as regards wave sequence and conformity in all the leads.

The *x*-ray examination defines the left margin of the heart sloping towards the apex region in the sixth intercostal space, 4½ inches from the mid-sternal line; the aortic shadow is abnormally wide—namely, 3½ inches; its margins are blurred and irregular; a pulsating swelling, similar in density to the cardiac shadow, and apparently continuous with this latter, is seen to extend 3½ inches to the right of the mid-sternal line, its edge, sharp and clear, stretching inwards at its superior extremity to join the aortic shadow at an acute angle, its lower margin, distinctly above and separated from the diaphragm, blending imperceptibly with the inferior aspect of the cardiac shadow; the lungs appear to expand normally, and the range of diaphragmatic movement is unimpaired.

Simultaneous curves recorded on a rapidly moving drum from small receivers placed over the apex and the pulsating tumour to the right of the sternum indicate that the impulse in each region is an outward thrust, and measurement makes it clear that the movements are not synchronous; the apex beat, by a fraction under a fiftieth of a second, being the prior event.

The urine was normal in every respect. The Wassermann test was positive.

Discussion of Diagnosis.

The condition was thought to be an intrapericardial aneurysm of the aorta; and in arriving at this diagnosis one was largely guided by the following considerations:

1. The punctate heaving quality of the pulsation, which to palpation appeared synchronous with the arterial pulse.
2. The presence of aortic reflux, which, in view of the positive complement fixation test, would suggest syphilitic disease of the aortic stem, and the conduction of the diastolic murmur from its seat of production over the entire region of the tumour and upwards into the cervical vessels.
3. The fact that the aortic root and the first 2 inches of its ascending arch are situated within the confines of the pericardial sac.
4. That the direction of least resistance to the spread of a dilatation aneurysm proceeding from the aortic root would be downwards within the cavity of the pericardium.
5. The fluoroscopic appearances which identified the shadow of the tumours with that thrown by the heart and great vessels, and the distinct line of continuity which connected the marginal extremity of the tumour with the right-hand border of the ascending aorta; also the definite character of the expansile pulsation which seemed to warrant the exclusion of new growth or encapsuled pericardial effusion.
6. The absence of pressure signs, which, moreover, would be hardly likely to complicate the early stages of an aneurysm originating within, and governed in the matter of the direction of its spread by, the pericardial investments.

After-History and Progress.

Considerable relief to the subjective symptoms was noted during the first three months of treatment, for which, no doubt, physical rest was mainly responsible; there was, however, no material improvement; the aneurysm was palpably increasing in size, a note of February 18th, 1921, giving its outer border a distance of 4½ inches from the mid-sternal line, and the patient was at that time complaining of sharp attacks of pain with the least effort, also cough and a feeling of suffocation, the latter aggravated by any attempt to assume the recumbent position. A month later the outer border of the impulse extended 5¼ inches from the mid-line, and examination at this time made it clear that pressure was being exerted on the right bronchus, and, further, that the superior vena cava was suffering obstruction. During April the symptoms increased in intensity; the cough, more especially troublesome at nights, the violent pain and the insomnia combining, at this time, to produce an extreme degree of debility and physical exhaustion; the outer border of the impulse was then to be found extending a distance of 5¾ inches from the mid-line; moist sounds were heard at both pulmonary bases; the air entry to the right lung was diminished.

During the last fortnight of life expectoration was profuse, and every paroxysm of coughing was accompanied by violent

and intense prostration. On May 13th the sputum became tinged with blood, and several small recent clots were expectorated. The patient died next day.

Autopsy Findings.

The two layers of the pericardium were found to be closely adherent, and numerous firm adhesions united the pericardial surface to the pleura on each side. The pleural cavities were in great part occupied by dense adhesions in the neighbourhood of the pericardium, but on separating these on the right side the cavity was found to contain a large amount of recent blood clot.

The heart was considerably enlarged; the aortic valve was incompetent; the cusps of the aortic valve, more especially the anterior and right posterior, were thickened, retracted, and distorted; there were no obvious vegetations; the wall of the aorta showed extensive atheromatous changes, the macroscopical appearances indicating an advanced degree of the process. Immediately above the aortic valve, at the junction of the anterior and right posterior cusps, a large saccular aneurysm measuring 4½ inches by 4½ inches arose; it was completely covered by the adherent layers of the pericardium, and it was about two-thirds full of laminated clot; its upper aspect was adherent to the right pleura and lung, which had suffered much dislocation, and here it was that the aneurysm had ruptured into the adjoining pleural cavity and pulmonary tissue.

THE PRESENT VALUE OF THE WIDAL REACTION IN THE INOCULATED SUBJECT.

BY

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AN acutely febrile case was recently admitted to the Princess Alice Hospital, Eastbourne, on which I was asked to perform a Widal reaction. The technique used was Dreyer's macroscopical method with the Oxford standard cultures. The result read as follows:

CASE I.

	Serum Dilutions.			
	1 in 25.	1 in 50.	1 in 125.	1 in 250.
Typhoid cultures	+	+	+	+
Paratyphoid A	Trace	–	–	–
Paratyphoid B	–	–	–	–

The reading was "strongly positive for typhoid."

The patient was an ex-soldier, inoculated for enterica during the war, the last time most likely in 1917. The clinical signs were those of continuous fever with some physical signs in the chest, and a provisional diagnosis of pneumonia had been made. The case was subsequently regarded, on the strength of the Widal reaction, as typhoid fever, probably pneumonic in type, it being assumed that the war-time inoculins had died away by this time.

The day after the test the patient was removed to the Borough sanatorium as an infectious febrile case. He died some days later. Clinically the symptoms were not typical of enteric, and a *post-mortem* examination was performed. Miliary tubercle was found to be the cause of death. It was then suggested by Dr. W. G. Willoughby (M.O.H. for Eastbourne), under whose care the case had been, that the positive Widal reaction might have been due to residual effects of war-time inoculation. I reported the case to two leading authorities for their opinions. One of them held that miliary tubercle may accentuate any existing agglutinins. He also pointed out that miliary tubercle and enteric may coexist, and that he had had a case of this kind where Peyer's patches showed no signs of inflammation yet where culturally 50 per cent. of the colonies in the mucous membrane of the lower part of the small intestine agglutinated with paratyphoid B serum in high dilutions, the blood of the same case also giving a highly positive Widal reaction to paratyphoid B, on which alone a diagnosis was made. The second authority offered the opinion that it was quite possible that "residual" agglutination could account for my results, but that one would expect, if this were so, a lower titre of agglutination than 1 in 250 after four or five years unless the man had given a very high response to his inoculations.

In order to prove what degree of residual agglutinins occur normally I estimated the agglutinin reactions to typhoid, paratyphoid A, and paratyphoid B of five healthy ex-soldiers, with the following very instructive results:

CASE II.

	Serum Dilutions:			
	1 in 25.	1 in 50.	1 in 125.	1 in 250.
Typhoid cultures	+	+	+	+
Paratyphoid A	–	–	–	–
Paratyphoid B	–	–	–	–

This case had had Flexner dysentery in 1916, and agglutinated Flexner's bacillus up to 1 in 250.

CASE III.

	Serum Dilutions:			
	1 in 25.	1 in 50.	1 in 125.	1 in 250.
Typhoid cultures	+	+	+	Trace
Paratyphoid A	+	Trace	–	–
Paratyphoid B	–	–	–	–

CASE IV.

	Serum Dilutions:			
	1 in 25.	1 in 50.	1 in 125.	1 in 250.
Typhoid cultures	+	+	+	Trace
Paratyphoid A	–	–	–	–
Paratyphoid B	Trace	–	–	–

CASE V.

	Serum Dilutions:			
	1 in 25.	1 in 50.	1 in 125.	1 in 250.
Typhoid cultures	+	+	–	–
Paratyphoid A	–	–	–	–
Paratyphoid B	–	–	–	–

CASE VI.

	Serum Dilutions:			
	1 in 25.	1 in 50.	1 in 125.	1 in 250.
Typhoid cultures	+	+	–	–
Paratyphoid A	–	–	–	–
Paratyphoid B	–	–	–	–

We thus have a fairly complete answer to our queries. Fifty per cent. of the cases agglutinate typhoid up to 1 in 250, so that such a high response is no uncommon thing in the inoculated after four or five years. Paratyphoid agglutinins are very slight in all cases as compared with typhoid residua. The explanation of this no doubt lies in the greater strength of the typhoid vaccine given and possibly also because this was used alone at first during the war.

I cannot agree that the existence of miliary tubercle accentuated any potential agglutination titre, otherwise the paratyphoid titres in Case I should have been higher, but of course one cannot generalize too much from these few cases.

The essential point of the matter is that a positive Widal reaction in the inoculated subject, even some four or five

years after inoculation, *is of no diagnostic value whatever in typhoid fever and is of very doubtful value in paratyphoid fevers unless of markedly high titre. But this in no way detracts from the superlative value of the reaction in the non-inoculated.*

A repetition of the reaction after several days' interval is, as a rule, not sufficiently decisive in everyday work to recommend itself to those of us who must, if possible, supply a rapid and unequivocal answer to our colleagues in the wards, but where this can be done it is sometimes helpful as an aid to diagnosis, but no more. Finally, this note illustrates very clearly the need for close co-operation between the pathologist and the physician in all obscure cases of this nature.

I am indebted to Dr. A. Deane, Surgeon to the Princess Alice Hospital, and also to Dr. W. G. Willoughby, Medical Officer of Health for Eastbourne, for their helpful suggestions and for their permission to report the original case; likewise to Dr. Dennis Embleton and Dr. A. D. Gardner for giving me the benefit of their wide experience in these matters.

LAPAROTOMY FOR INTESTINAL OBSTRUCTION ON BOARD SHIP.

BY

VINCENT MOXEY, M.R.C.S., L.R.C.P.,

SURGEON TO THE ROYAL MAIL STEAM PACKET COMPANY.

LAPAROTOMIES on board ships of the mercantile marine are perhaps sufficiently uncommon to be worthy of record, and the case related below presents certain points of interest:

During the voyage of the R.M.S.P. *Desna* from Liverpool to Buenos Aires, on the day after leaving Lisbon (August 20th), a Portuguese lad, aged 17, went down with abdominal pain and vomiting. He was seen by Dr. Serao de Carvalho, the Portuguese surgeon, and the condition was provisionally diagnosed as intestinal colic. Next day he was no better, and Dr. Carvalho concluded that the case was one of intestinal obstruction and asked me to see him.

Dr. David de Sarmento, professor in the faculty of medicine, Lisbon, who was a passenger on board, also very kindly joined us. We found all the classical signs of intestinal obstruction present, and the question was whether the causation was volvulus, intussusception, or strangulation of the internal hernial type. As the patient seemed to be relatively well—that is, not so severely ill at the moment as one would have expected—the possibility that it might be one of those uncommon cases of pseudo-strangulation such as is described by Lejars (*Medicina de Urgencia*, Oddo, p. 375) crossed one's mind. Perhaps the wish was rather father to the thought, as operation under the conditions was not particularly attractive. Anyhow, valuable time was wasted with no results. By the evening of August 23rd it was clear that intervention was imperative, but, his state being still fair, it was left until the morning of the 24th.

He was taken to the ship's operating theatre; Dr. Carvalho gave chloroform, and Dr. Sarmento was good enough to assist me. On opening the abdomen, by an incision four inches long a little to the left of the umbilicus, the enormously distended and congested small intestine protruded in a troublesome fashion. A considerable quantity of sero-sanguinolent peritoneal fluid escaped, and patches of lymph were to be seen on the visceral peritoneum. It was not difficult to bring the seat of the trouble into view—a knuckle of ileum, about two feet from the caecum, was incarcerated in a mesenteric pocket; this was withdrawn. The condition of the compressed portion, about three inches long, was not encouraging, and one now regretted not having operated earlier. Had the loop been a longer one it would surely have been gangrenous, whereas this one was small and comfortably supported all over its surface, and had avoided the deadly venous congestion of the ordinary hernia. It looked just possible to avoid resection, and I decided to chance it, as excision of a piece of intestine, with the central end in the condition it was, would probably have been disastrous anyhow. Further, a temporary anus seemed almost as risky. The protruded intestines were replaced, no flushing of the peritoneal cavity was employed, and the abdominal wall was sewn up in the usual three layers. This latter, owing to the vagaries of Father Neptune, was the most tiresome part of the whole procedure. Still, the weather was very good; we were about the latitude of Cape Verde, and there was only a moderate swell on. Simple dressings, sterilized on board, were applied and kept in place with a many-tailed bandage.

During the ensuing night the patient passed flatus, and next day a large motion. He then started eating well and with a good appetite. There is nothing further to relate of any moment, save that an abscess of the abdominal wall had to be evacuated a few days later, by loosening the two lowest stitches. Foul faecal-smelling pus escaped, evidently due to infection of the wound by the peritoneal contents. On September 7th he was landed in Buenos Aires in good condition, the abdominal incision almost healed.

Surgery at sea raises many interesting questions, which it is not possible to discuss here. But the ship's surgeon must be prepared, above all, to open an abdomen if necessary, as this is obviously the most likely form of urgency to be met with. It therefore behoves him to have ready in his mind the requisite plan of campaign, the best place to operate, likely assistants, the anaesthetic, the simplest ways of dealing with the conditions found, simple dressings, and arrangements for after-treatment.

Memoranda:

MEDICAL, SURGICAL, OBSTETRICAL.

"HAEMORRHAGIC" CHICKEN-POX.

THE following personal history may interest Dr. Wanklyn (November 18th, p. 977). When within three months of my final examination I saw in the Sick Children's Hospital a case of chicken-pox. The child was isolated in a side room awaiting transfer to the fever hospital, and the physician showed the case to a few students and asked for a diagnosis. I was in the room for about one minute and did not touch the patient. Exactly fourteen days later I began to feel rather seedy and the idea occurred to me that I had got chicken-pox. I stayed in bed and looked anxiously for the rash next day, but nothing was to be seen. On the second day, however, a few characteristic spots were present. Not more than a dozen appeared in all, but haemorrhages took place into several of the larger vesicles. I do not think there was any surrounding ecchymosis. There is still a faint scar from one on my wrist. Slight fever and malaise for a couple of days constituted the whole illness. I was much too annoyed to let a real doctor see me, but I think Dr. Wanklyn may take it that the diagnosis was correct.

W. F. SHANKS, M.B., Ch.B.

University of Glasgow, Physiology Department.

ACUTE MENINGITIS FOLLOWING INFLUENZAL MASTOIDITIS.

As acute meningitis, following aural suppuration, is always looked on, and unhappily rightly so, as a fatal complication we venture to publish the following report. We regret that the exigencies of the case did not allow of a bacterial examination of the cerebro-spinal fluid.

G. E., aged 7, developed influenza during the March epidemic of this year. Pain in the right ear was complained of on the third day, with gradual increase, until discharge was noticed on the sixth day. Except for the aural discharge no other sign or symptom was noted though carefully looked for, and the child rapidly convalesced, when measles developed on the thirteenth day.

The measles took a normal course, and on the nineteenth day the child was apparently well, sitting up and playing with toys. The aural discharge continued, but there were no mastoid symptoms whatever, when suddenly on the twenty-first day the child complained of deep pain behind the ear, and two hours later typical cerebral vomiting commenced. Five hours later we found the child collapsed with clammy skin, roused with difficulty and then very irritable. There was marked photophobia with right external squint. There were no external mastoid symptoms and no tenderness; the discharge was profuse and ropy, the drum red, and the posterior inner meatal wall red and swollen. Marked head retraction was present, Kernig's sign positive, and vomiting frequent.

An immediate operation was advised and carried out under light anaesthesia given by Dr. J. F. Walker. The mastoid was of the pneumatic type and bathed with pus throughout, the intercellular bone being largely necrosed and easily removed; the lateral sinus was inflamed and granulated. On removing the tegmen antri a bulging dull red dura was exposed, and on making an opening into this much very turbid fluid escaped under pressure. The posterior cranial cavity was similarly drained in front of and below the sinus, a small wick drain being left in each fossa. The whole operation occupied nine minutes, as speed was in our opinion most necessary.

Next day the child was given 12½ c.cm. of polyvalent anti-streptococcal serum, a similar dose being injected on the five following days. The dressing was changed daily, also the wick drains. For two days the condition was extremely serious; all the meningeal symptoms remained, but the vomiting was even more persistent. Slight improvement was noticed on the third day, and it continued till the eighth day, when all meningeal symptoms had disappeared and a complete recovery eventuated.

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W. H. SARRA, M.R.C.S., L.R.C.P.,
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IN a recent visit to Guatemala and other countries of Central America Professor Fülleborn, of the Hamburg Tropical Institute, found that 90 per cent. of the Indian labourers in the coffee plantations were suffering from ankylostomiasis.

Reports of Societies.

BLOOD TRANSFUSION IN CIVIL PRACTICE.

AT a meeting of the Medical Society of London on November 27th, with Lord DAWSON OF PENN (President) in the chair, a discussion took place on "Blood transfusion in civil practice."

Mr. GEOFFREY KEYNES, who introduced the subject, exhibited the title-page of the earliest monograph on transfusion, published in Italy in 1668. The practice, he said, was in abeyance in the eighteenth century and was revived in the nineteenth. The literature was now growing very fast, and the great majority of contributions in recent years had been American. Earlier methods were by direct transfusion, which the speaker regarded as being now only of historical interest. There were at present two schools of technique, one of which held that whole blood was the more desirable, while the other insisted upon the use of an anticoagulant. Whole-blood methods were satisfactory in the hands of those accustomed to them, but anticoagulant methods, depending upon the employment of solution of sodium citrate, were most satisfactory for general use, and it was these which had popularized transfusion. A good many fatalities followed transfusion in former years, and the cause was supposed to be the introduction of air bubbles into the circulation, but a certain small amount of air could be introduced without harm, and it was probable that in most of these cases incompatibility of bloods was the responsible factor. Post-transfusion reactions were occasionally severe, owing to gross incompatibility, but there were also a number of slight reactions following the transfusion of compatible bloods, and suggested causes for these were;

(1) The anticoagulant; (2) incipient clotting; (3) effect of anaesthetics on serum; (4) "minor agglutinins"; (5) protein shock; (6) distilled water for dissolving anticoagulant.

These slight reactions were of no very great importance; he had never seen them interfere with the efficacy of the method, and it was not necessary to be alarmed even with a rise in the pulse rate to as high as 150. In addition, moderate reactions had been noted attending second or later transfusions, the causes of which were induced incompatibility and possibly true anaphylaxis. The disquieting thing about these moderate reactions was that they could not be eliminated even by the most careful grouping of bloods, but they did not seem to happen often enough to make necessary the abandonment of transfusion on account of the danger. It was well never to use the same donor twice, if possible, and to ensure that blood of the same group as that of the recipient's blood was always used. He classified the indications for transfusion as follows (italics indicate that in those cases transfusion is of less importance or of doubtful value):

Haemorrhage and Shock: Traumatic haemorrhage, ectopic gestation, post-partum haemorrhage, gastric ulcer, etc.
Pre-operative: Debility or cachexia, haemorrhage.
Post-operative: Following severe operations. Cases involving much loss of blood are more benefited than those suffering purely from post-operative shock.
Haemorrhagic Diseases: Haemophilia, melaena neonatorum, *jaundice, purpura.*
Blood Diseases: Pernicious anaemia, *leukaemia.*
Toxaemias: Pyogenic, severe burns, *carbon monoxide and nitrobenzol and benzol poisoning.*

Blood transfusion was a very useful therapeutic measure, though its limitations were quite definite. In this country its use was restricted owing to the absence of any system of professional donors, such as existed in America, and possibly also to an exaggerated idea of the technical difficulty.

Mr. GORDON TAYLOR, who had a preference for the whole-blood method, said that he had seen only one case of post-transfusion reaction. During the last three years he and colleagues associated with him had done nearly one hundred transfusions. In cases of pneumococcal peritonitis very favourable results had been reported from blood transfusions, and in at least one such case within his own experience the result had been almost dramatic. From what he had seen in that case and in one or two others he would be disposed to go on using blood transfusion from the moment of the septicaemic onset. In operations of magnitude he had used blood transfusion several times with very good results. Pre-operative transfusion had been used successfully in malignant disease of the stomach and bowel. In ten cases of bleeding gastric ulcer, in which haemorrhage continued in spite of medical treatment, partial gastrectomy was done, and the patients were transfused either before, during, or after operation, with recovery in nine of the cases.

Dr. A. E. Gow said that in cases of pernicious anaemia in which the blood picture of the first attack suggested that the anaemia was due to increased haemolysis, as apart from the distinctly aplastic type, a single transfusion of 600 to 800 c.cm. of citrated blood was usually of benefit. The result was far more rapid than with arsenical medication alone. The choice of donor was important if a powerful reaction was to be avoided. In the aplastic type of pernicious anaemia transfusion might stimulate the marrow to activity, though the effect was temporary. The transfusion acted as a "strike-breaker" for a time, but the "strikers" eventually gained the day. It was better in these cases to give a small dose of not more than 200 c.cm. and repeat it in five or seven days, rather than to transfuse a larger quantity.

Dr. ALEX. FLEMING described the technique employed in the transfusion of defibrinated blood, which he and his colleagues at St. Mary's had used recently in place of the citrate method. Sir Almroth Wright had been doing what he called immunal transfusions in septic cases during the past few months, using defibrinated blood, to which was added a very small quantity of a vaccine, giving an increase in the antibacterial content to the staphylococcus or streptococcus, and after the blood was introduced there was an almost immediate increase, which could be tested, in the bactericidal power of the recipient's blood.

Sir THOMAS HORDER expressed disappointment at hearing Mr. Keynes say that this was a therapeutic measure with very definite limitations. He still hoped that these limitations were not so definite, if only because he felt that any therapeutic method which did not put money into the pockets of wholesale chemists was one that deserved exploiting to the utmost. With regard to gastric ulcer, he was not sure that the extraordinary improvement which followed transfusion was due only to the effect upon the haemorrhage. He thought that the healing of the gastric ulcer was more rapid with transfusion than without it. In six cases of gastric or duodenal ulcer within his experience transfusion had been employed; the astonishing difference in the results he attributed to the type of the disease and the age of the patient, but generally speaking he was convinced that the ulcerative process itself was influenced. In ulcerative endocarditis, notoriously very disappointing in its therapeutics, he was coming more and more to believe that transfusion was a valuable method. He thought it more useful to give many small transfusions frequently than a few larger transfusions at longer intervals. He had seen benefit from transfusion in ulcerative colitis. In some of those difficult cases in which the colon seemed to be intolerant of chemicals and the patient of vaccines possibly small repeated transfusions might be of great value. In pernicious anaemia he had been disappointed, so much so that in his practice he did not transfuse in this condition unless the relatives suggested it and seemed disturbed because it was not done.

Mr. KENNETH WALKER had been struck by the extraordinary result that followed the transfusion even of a very small quantity of blood. Sometimes it had been possible to use only 200 c.cm. in bad surgical cases, and yet the results had been altogether out of proportion to the amount of blood used. He emphasized the importance of fluids to supplement blood transfusion in cases where there had been haemorrhage and severe shock. The blood appeared to "fix" the fluid in the veins and prevent the transudation which occurred when using saline alone. There was no branch of surgery in which blood transfusion had greater scope than in genito-urinary cases. From American literature it appeared that good results had followed in uraemia from a combination of venesection, blood transfusion, and saline injections. He favoured the citrate method on the ground of simplicity.

Mr. EARDLEY HOLLAND said that in obstetrics and gynaecology, while he could not get on without blood transfusion, the cases in which he employed it were fewer than formerly. At the London Hospital its use had been given up in acute puerperal sepsis. Haemorrhages in obstetrics and gynaecology might be divided into two groups: (1) acutely arising haemorrhages in otherwise normal cases, of which ectopic gestation was an example, and (2) repeated haemorrhages, of which examples were placenta praevia and secondary *post-partum* haemorrhages due to sloughing of deep tears of the cervix. In the former, while blood transfusion was useful, the opportunity was not always forthcoming, neither donor nor apparatus being immediately available; but in the latter, the patients being in no state to withstand the slightest additional

shock, blood transfusion was extremely valuable, and, in the nature of the case, more practicable also. He had rarely seen a case of ectopic pregnancy in which transfusion was essential for saving life.

Mr. KEYNES, in a brief reply, said that in a good many surgical cases transfusion might be a luxury, but undoubtedly operative risk was reduced, even though it was not possible to say that a patient would have died if there had not been transfusion. In the technique rapidity was not of first importance; he had given citrated blood twenty-seven hours after it had been taken from the donor, and the result was as good as if it had been given immediately, and there was no reaction whatever.

EPIDEMIOLOGY OF SCARLET FEVER.

AT a meeting of the Section of Epidemiology and State Medicine of the Royal Society of Medicine held on November 24th, the President, Dr. R. J. REECE, in the chair, Dr. F. M. TURNER read a paper on the age and sex distribution in scarlet fever. The author submitted a full biometric analysis of the statistics of age distribution amongst both notified cases in London and cases admitted to the Metropolitan Asylums Board's hospitals, together with tables relating to certain provincial cities. Notwithstanding the general similarity of the figures from year to year, it was possible to show that the age distribution differed more than would be expected, were the fluctuations random, in successive years. The mean age of females in notified cases was always higher than that of males and, with one exception, in the admitted cases. The mean ages of cases notified uniformly exceeded that of cases admitted. The statistics showed a general tendency for the mean age to increase with the prevalence, although the arithmetical value of the coefficient of correlation between mean age and number of cases notified was small. The mean age had increased over the period studied (1887–1922). Manchester statistics likewise showed an apparent increase of mean age in periods of prevalence and a general increase of mean age through the series.

In opening the discussion on the paper, Dr. HAMER pointed out the existence of a tendency for the mean age and the prevalence to increase together in the case of small-pox mortality statistics. In his view the phenomenon was dependent upon changes in the amount of susceptible material in the population; this explanation he was sure best accounted for the epidemiological course of measles. Measles was an easy case, influenza a very difficult one, scarlet fever fell between the two. Dr. ISSERLIS, in commenting upon the statistical aspects of the paper, remarked that the application of the theory of sampling to a problem such as this involved theoretical difficulties, so that it was necessary to be particularly cautious in drawing inferences as to the limits of chance fluctuations. Dr. MAJOR GREENWOOD congratulated the author on his valuable contribution to biometry; he suggested that the smallness of the coefficient of correlation between prevalence and mean age might be due to non-linearity of regression, so that the prima facie inference that the correlation was a real one might be justifiable. The biological interpretation of this suggested by Dr. Hamer seemed the most feasible one. Dr. BROWNLEE said that it was essential to bear in mind the factor of mass of infection; whenever the mass of infection was great—for instance, in milk epidemics—the mean age of attacked persons was high. Dr. MCVAIL inquired whether the excessive incidence upon females might not be accounted for by the greater proportion of females in the general population at susceptible ages. Dr. BUTLER commented on the difference between the age incidence in a disease such as scarlet fever to which the whole population was not susceptible and that of a disease such as small-pox attacking an unvaccinated population. It appeared that in the former case immunity came with age and that an accumulation of susceptible material was not the whole explanation. Dr. TURNER, in replying, remarked that an obvious and possible explanation of the higher mean age of females attacked was that the girls nursed children in the interval before the latter were removed to isolation hospitals.

Dr. JOHN BROWNLEE then read a communication on the relation between rainfall and scarlet fever. He exhibited an extensive series of charts which led him to conclude that the influence of deficient rainfall upon the prevalence of scarlet fever, to which the late Dr. Longstaff had devoted special study, was not a direct one. There was some evidence that if a period of deficient rainfall coincided with the epoch at which, from a study of the periodicity of the disease, an epidemic was to be expected, the rainfall deficiency increased the magnitude of the epidemic. Deficiency of rainfall was not, however, a sufficient single cause of an epidemic. Sir GEORGE BUCHANAN inquired whether the English rule that scarlet fever was an autumnal epidemic were universal and whether grouping rainfall in smaller than annual units had been tried. Dr. BROWNLEE said that the case in favour of deficiency of rainfall as a precursor was not strengthened but weakened when a fine time unit was adopted.

THERAPEUTICS OF QUINIDINE.

A MEETING of the Liverpool Medical Institution was held on November 16th, with the President, Dr. J. HILL ABRAM, in the chair, when Dr. JOHN HAY read a paper on the after-results of quinidine in disorderly action of the heart. He reported the results of treatment with quinidine in 21 cases; 13 of these had been described in an earlier communication to the society, and of the 13 cases only 3 had retained a normal rhythm. During the last seven and half months quinidine had been administered to 8 additional patients, and in each case the fibrillation had been broken and a normal rhythm restored. Four, however, had relapsed. In all there were 6 complete failures; 8 cases had relapsed after temporary cessation, and 7 patients had maintained a normal rhythm. Not included in the above series were two recent responses to quinidine, but it seemed to him a little early as yet to include them in the successes. Dr. Hay discussed the type of cases suitable for treatment with quinidine, and also the type of case in which the exhibition of that drug was unjustifiable.

Dr. A. DOUGLAS BIGLAND described observations made by Dr. Voigt and himself on patients treated with quinidine. Out of 7 cases of auricular fibrillation 2 had regained normal rhythm and maintained it up to the present, over periods of six and five and a half months respectively. One case died suddenly after having had a normal rhythm for five weeks. Two cases had relapsed and were still under observation, while two other cases were not able to continue the treatment.

Dr. I. HARRIS considered there were three striking facts in connection with quinidine: (1) Provided that the drug was given long enough and in sufficient quantities, in a great majority of cases a normal rhythm could be restored. (2) There was a pronounced tendency to relapse after a normal rhythm had been restored. (3) The sudden restoration of the normal rhythm effected by quinidine favoured embolism. The drug as such was not dangerous. He had given the drug in normal cases without observing ill effects. Dr. Harris considered that there was another factor in the treatment by quinidine which might bring undesirable results. In the great majority of cases of fibrillation the pressure in the veins was greatly increased, which suggested that the total output of the heart was diminished and the strain on the heart muscle correspondingly lessened. To restore the rhythm meant increased output and increased strain on the heart muscle. Dr. Harris was of opinion that, since quinidine was a dangerous drug and did not influence the heart disease itself, it was questionable whether it was worth while endangering the patient's life for the sake of restoring the normal rhythm, considering that in many instances, after a shorter or longer period, fibrillation returned. He thought that further observation was necessary before a definite conclusion could be arrived at regarding the value of quinidine in fibrillation.

Blood Transfusion.

Mr. J. T. MORRISON read a paper on two cases treated by blood transfusion.

The first patient, a girl 5½ years old, subject to nose bleeding, had a very severe epistaxis one week before admission to hospital. On admission her nose was bleeding in spite of having been plugged. Her pulse rate was 176, her temperature 99.6°. She was blanched, and her haemoglobin was below 20 per cent.; the white blood corpuscles numbered 44,650, no abnormal types being present. There were purpuric spots on her back and legs. The cervical glands were enlarged (perhaps from recent impetigo), the spleen was palpable, the liver apparently normal. The treatment given was horse serum, 10 c.cm. subcutaneously, and calcium lactate, 10 grains four-hourly. During the following three days there was no improvement; indeed, there were further haemorrhages. After four days transfusion was decided on, her condition being desperate (pulse rate 164). To supply the supposed missing factor in coagulation without unduly raising the blood pressure only 50 to 60 c.cm. of blood were used. The father of the patient was the donor, his red cells having been previously tested. The technique used—as the

quantity was so small—was the multiple syringe method: 20 c.cm. Record syringes, dried with ether and sterilized in liquid paraffin, were employed. The blood was injected into the external jugular vein of the patient, the vein being exposed under local anaesthesia. Great improvement followed, and the transfusion was repeated the following day; convalescence thereafter was uninterrupted. The patient had had an operation safely since.

The second case was a boy, aged 6, who had had tonsils and adenoids removed, with a good deal of reactionary oozing for the first two days. On the third and fourth days there was no more oozing; on the fifth day, however, there was a sharp haemorrhage from the post-nasal space. Calcium lactate and horse serum were given as in the previous case. The sixth day was uneventful, but on the seventh day bleeding began again and oozing was very persistent. A dangerous degree of anaemia was soon reached. The case was regarded as one of secondary haemorrhage, but transfusion was tried in spite of the fact that the source of the bleeding could not be controlled. Between 50 and 60 c.cm. were given, as already described, from a No. 4 blood donor, and immediate improvement was obtained. There was no further bleeding, but it was thought advisable to repeat the dose on the next day, and no further trouble of any kind ensued.

Mr. Morrison concluded by saying that this experience confirmed some of the indications for transfusion now beginning to be recognized—namely, the haemorrhagic diseases, including melaena neonatorum and haemophilia, CO and benzol poisoning, and, above all, desperate cases of primary haemorrhage. Except in the last named, the amount transfused need not be large.

Observations on General Anaesthetics.

Dr. MINNITT read a paper entitled "Some observations on general anaesthetics." He explained what ethanesal was and how it was obtained, and, in reviewing his experience of about 300 cases, he contrasted its advantages and disadvantages as compared with ether, the result being greatly in favour of ethanesal. He pointed out important matters in connexion with an induction, laying stress upon full anaesthesia being obtained before operative interference began. He then described his observations with regard to blood pressure during operations, and showed how there was a normal graphic record in ordinary cases. He compared the differences from this normal graph with the variations in difficult cases, and showed that these observations would be valuable to both the anaesthetist and the surgeon. He instanced McKesson's interpretation of blood pressure findings, and suggested treatment in the case of patients having a poor blood pressure, emphasizing the value of heat, administrations of oxygen, and hypodermic injections of pituitrin. Dr. Minnitt exhibited a specimen of a hot-water bottle to warm the air breathed from the mask by the patient. Slides were also shown depicting the influence of oxygen and pituitrin upon falling blood pressure. Gas and oxygen anaesthesia was discussed, and Boyle's apparatus and a No. 8 Ohio monovalve apparatus were shown.

Dr. G. F. R. SMITH confirmed Dr. Minnitt's favourable opinion of ethanesal, but was doubtful if its advantages over ether rendered its use in hospital practice justifiable in view of the greater expense. Dr. Smith thought that equally good results could be got with nitrous oxide and oxygen, with simpler and cheaper apparatus than those on the market. He gave a word of warning in regard to the danger of that method in major surgery.

ACUTE NEPHRITIS.

A MEETING of the Manchester Pathological Society was held on Wednesday, November 8th, when Professor SHAW DUNN read a paper on some aspects of acute nephritis.

Professor DUNN referred to the impetus which the study of the minute morphological changes in the kidney in acute nephritis had received of recent years—on the one hand through the wealth of material afforded by the appearance of the disease in epidemic form in the armies of the western theatre of war; on the other hand by the acquisition of a fuller knowledge of the minute structure of the normal kidney. The modern conception of the kidney as an organ composed of nephrons or units each composed of a glomerulus and tubule, with a blood supply rather more than less of their own, had an important bearing on the interpretation of diseases of the organ. The correlation of disturbed anatomy and disordered function became more interesting and more fraught with possibilities and with clinical profit.

Histologically, the majority of cases of nephritis dying in the acute stage showed predominantly a diffuse glomerulo-nephritis. This had been the case not only in the war necropsies but in civilian practice as well. The glomerular capillaries were blocked by proliferated endothelium and leucocytes; thus the lesion was vascular. At times there occurred in addition catarrh and accumulation of desquamated cells in Bowman's capsules, this type of lesion generally being more destructive to the kidney as a whole.

Professor Dunn analysed the results of his investigations on the kidney, both in cases clinically diagnosed as acute nephritis and also in a further series where no special renal disturbances had been noted during life, but where the naked-eye appearances had led him to make detailed studies. In two cases with oedema, dying of uraemia and coming to necropsy, a diffuse glomerulo-nephritis was present of such degree as to give the impression that renal function had been largely arrested. The cases which were incidentally discovered at necropsy fell into two histological groups. A small group corresponded closely to Gaskell's focal embolic nephritis, plugs of thrombus being found in the glomerular capillaries. The second type showed a condition similar in kind to that exhibited by the uraemic cases, but less in degree. It was interesting to note that these latter all occurred in cases dying of sepsis of some kind, and it appeared that this was a most important factor in the causation of diffuse glomerulo-nephritis. On the extent of such a glomerulo-nephritis—an extent varying from case to case—depended the presence and quality of physical signs of kidney disease. In those cases where bacteriological examinations were carried out the infecting organism was found most commonly to be the haemolytic *Streptococcus pyogenes*.

DEMENTIA PRAECOX.

A MEETING of the Ulster Medical Society was held in the Medical Institute, Belfast, on November 16th, with the President, Mr. R. J. JOHNSTONE, in the chair, when Dr. W. CALWELL read a paper entitled "Dementia praecox from the ordinary physician's point of view."

Dr. Calwell drew attention to the claim that this type of case was a distinct group in insanity, just as one hundred years ago the same claim was made for general paralysis of the insane, a claim now fully substantiated. Kraepelin's classification of mental diseases, based on age at onset, general course, peculiar symptoms, progress, and termination, was an advance on the older one, based on mental symptoms alone; but, just as in skin diseases, it would, he believed, ultimately give place to a classification based on pathological findings. Kraepelin's guiding points in dementia praecox—the age of adolescence at onset, the progressive but intermittent course, the hopelessness of prognosis, and ultimate termination in complete dementia, with absence of direct fatal termination—had all many exceptions. The onset was generally slow and insidious, but little or no reference had been made to the question of any preliminary illnesses; this was a subject that required investigation, and that could be carried out only by the practitioner in charge of family work. If a case of infantile paralysis or of encephalitis lethargica was seen a year after onset, it would be difficult to reconstruct the initial trouble. Long lists of symptoms could be made; perhaps some sort of order could be evolved by a study of psychology and by the application of Hughlings Jackson's dicta that in degeneration the higher levels went first and were marked by a loss of function of this level and an uncontrolled action of the lower. It must, however, be remembered that the destruction in that case was so slow as to be imperceptible, like the hour hand of a clock; and, while that destruction was taking place, it was accompanied by a certain amount of perversion, such as would be expected from the slow, minute deterioration found in the nerve cells. Besides, there were no clearly defined authorities in the mental hierarchy, one above the other, but a gradual evolution from the projection centres in front of the Rolandic fissure, forward to the intermediate, and then to the frontal and the pre-frontal areas, where the motor type of cell seemed to act as the physical basis of will, conation, and the sense of effort, as well as of high intellectual concepts requiring a motor basis. Similarly, the sense of sight rose in evolution as it spread forward from the occipital lobes, and of hearing as it spread from the Sylvian fissure. Much difficulty existed as regards diagnosis, as the delimitations had not been agreed upon, but the mentally deficient were always a stumbling-block. The extent of the disease was impossible to ascertain, as the name was not yet universally adopted, but 10 to 20 per cent. of admissions to asylums were of this nature, and as such patients lived and became more

markedly affected these institutions became crowded with them. Of the pathological theories advanced, that of Mott's seemed to bear a critical examination best—namely, a genetic weakness in the higher cortical cells, which yielded to any stress, physiological, psychological, or toxic, under the stimulation of the onset of puberty. The coincidence of the degeneration of the nerve cells in the cortex, of atrophy of the seminiferous tubes in the testes, and also of atrophy of the ovary, pointed to a cause acting on both nerve and reproductive organs, and seemed to ask for some close connexion. The testicular atrophy was much in excess of that found in other forms of brain degeneration. Prophylactic treatment should be entertained. Heredity existed in a very large percentage, but the infections of the mother when pregnant, influencing the thyroid, when the nervous system of the foetus was at a stage of critical development, should not be forgotten. The peculiar mental ataxia, or schizophrenia, where the perception, the intelligence, and the memory were but little impaired, but the emotion, the will, conation, interest, were markedly so, suggested an escape of the receptive cells, and a susceptibility of the motor type of cell, as was seen in infantile paralysis and in encephalitis lethargica. Dr. Rivers's suggestion of trying to discover the children who developed dementia praecox was valuable. Hope lay in prevention, and, perhaps, in very early treatment.

Colonel DAWSON said that the want of interest and emotion in the patient rendered cases of dementia praecox hopeless for suggestion as a treatment. He had, however, seen cases with all the manifestations of dementia praecox recover. As regards heredity, it had been stated that many of these cases were the offspring of general paralytics. He also pointed out that negativism meant an active reverse of the request, not merely a passive resistance. Professor LINDSAY and Dr. ADAMSON also spoke, and Dr. CALWELL replied.

EDINBURGH OBSTETRICAL SOCIETY.

THE first meeting of the eighty-first session of the Edinburgh Obstetrical Society was held on November 8th, the President, Dr. J. LAMOND LACKIE, in the chair. The President delivered his inaugural address, and drew attention to the fact that the mortality and morbidity among women in childbirth were no less than seventy years ago, and that childbirth was second only to tuberculosis as a cause of death among women. Such a state of matters could only be improved by close co-operation between the practical obstetrician and the laboratory worker—biochemist and bacteriologist—and by intensive training of students by actual residence in the maternity hospital and constant practice for a fixed period, including instruction in the ante-natal and post-natal departments, with subsequent attendance upon cases in the extern department. Unless the bedroom could be converted into a surgical operating room, every lying-in woman should be removed to hospital or nursing home. Each practitioner should have his private ante-natal department, and should regard it as his duty to exercise the closest supervision of every pregnant patient. He advocated a mixed diet during pregnancy, red meat being taken once or twice weekly, the necessary protein being obtained from eggs, fish, fowl, peas, beans, and nuts, with cereals. By limitation of fluids, especially milk, and of carbohydrates, according to the Prochownick method he believed it possible to obtain a smaller child with consequent diminution of the risk of dystocia. A timely induction of labour was often a far finer thing than the most brilliantly executed Caesarean section, which was too often the outcome of bungled midwifery. "Prophylactic forceps" as practised by certain American obstetricians he considered an unjustifiable proceeding, and advocated patient "standing by" combined with twilight sleep, provided pelvis, foetal head, presentation, and position were normal, as often yielding better results than the most brilliant abdominal or vaginal surgery. He now used forceps much less frequently than formerly and high forceps very seldom. Neither was he convinced of the value of the so-called Potter's version, which he looked upon as the best example of meddlesome midwifery, the introduction of which into this country as a routine method of delivery he would deeply deplore. The greatest need in the modern maternity hospital was a follow-up department to which the women should return, well or ill, for examination and advice. Much suffering might be prevented by early recognition and treatment of pelvic abnormalities resulting from parturition. Maternity insurance would also be of advantage in that it would tend to assure a period of proper convalescence.

Reviews.

CRIME AND PSYCHO-ANALYSIS.

THE author of *The Psychology of the Criminal*,[1] Dr. HAMBLIN SMITH, has had twenty-three years' experience as a medical officer in the English prisons, both "local" and "convict," and has given great attention during the last three years to the mental condition of offenders sent specially to him for examination and report from the courts at Birmingham, where he is chief medical officer of the prison. He is also lecturer on criminology at the University of Birmingham, and thus is specially equipped for undertaking to illustrate in this book the principle that "the intensive investigation of individual cases is the road to the solution of the problems of criminality."

The author deals with various aspects of his subject, but the most novel feature of the book is his discussion of psycho-analysis in relation to the criminal, and to this I propose to devote the greater part of the space at my disposal.

It may be said at once that a careful study of each individual offender's bodily and mental condition and behaviour, including as far as possible inquiry into his early mental history as evidenced by his conduct, is unquestionably an important desideratum in order to arrive at the best judgement on the questions whether he should be punished, and what, if he be rightly punishable, should be the nature of the penalty awarded. From a practical point of view it may be said further that the more we know of the individual offender the less we are concerned with what are so frequently and indefinitely alluded to as the "problems of criminality"; and all may agree with what the author in his first chapter somewhat obscurely lays down "as a fundamental position, that conduct is the direct result of mental life," etc. This dictum will scarcely at first sight be questioned by any psychologist to-day. Many years ago Dr. Charles Mercier persistently taught that a person's conduct is the main index to his mind, and that the careful study of his conduct is the essential preliminary to forming a judgement on the health or defect of his mental state. But much that is said in this book indicates that Dr. Hamblin Smith really means that study of the "mental life" is the necessary preliminary to a judgement on a person's conduct, and that the term "mental life" implies here the hypothesis of the "unconscious mind." In one place, indeed, he virtually sums up the matter of the problems of criminality in these words: "It follows that the real question is not so much what should be done to an offender in the way of punishment, but what can be done for him in the way of treatment," and proceeds to emphasize his view that the right method of studying "the psychology" of the criminal, or indeed of anyone, is to act on the Freudian hypothesis of the "unconscious mind." This "discovery" he ranks in value with those of Copernicus and Darwin. Each of these, he says, "changed our whole conception of our origin and destiny; but there has arisen another in this our time. Sigmund Freud, by his hypothesis of the unconscious mind, has radically altered all our views of human nature."

Two chapters—nearly half of the book—are devoted to the "offender's unconscious mind," and include an exposition of Freud's psychological doctrine and the method of applying it in practice now widely known as psycho-analysis, or as the new psychology, or, simply, as psychotherapy. Psycho-analysis is pronounced to be a science, and the discovery and elaboration of it to have been made in a scientific manner. The author is certainly to be credited with full success in his expressed endeavour to state fairly and dispassionately his own views on psycho-analysis, and most of the exponents of the Freudian teaching will probably accord him their approval. It is clear from what has been said above and from the trend of the last two chapters of the book that Dr. Hamblin Smith fully accepts the Freudian doctrine as indicating the best form of intensive investigation of individual cases, as the true road to the solution of the problems of criminality, and equally appropriate to the study of mental activities generally. It follows that an adequate notice of this book would require a more or less detailed consideration of the hypotheses the truth of which the author assumes as his postulate, though he

[1] *The Psychology of the Criminal.* By M. Hamblin Smith, M.A., M.D. Medical Officer of H.M. Prison, Birmingham; Lecturer on Criminology in the University of Birmingham, and at Bethlem Royal Hospital, London. London: Methuen and Co., Ltd. (Cr. 8vo, pp. vi + 182. 6s. net.)

admits that "there is much in psycho-analysis which is still highly controversial."

It is impossible within the limits of this notice to attempt an adequate criticism of the doctrines on which the author relies for his contentions. But it may be briefly noted that the hypothesis of the "unconscious mind," with all that it is held to imply by those who regard it as an established "discovery," is but an elaborate and complicated guesswork and wholly lacks scientific verification. One may search in vain in the writings of the originators and disciples of the various schools which hold this doctrine in common, however much they may differ *inter se* on more or less important details of practice, for anything like a clear setting forth even of the exact meaning they attach to the terms "mind" and "consciousness." Without some consensus on the extent and content of the fields of mind and of consciousness the concept of the "unconscious mind" is at least extremely nebulous; and, unless it be assumed that the innumerable processes of cerebration and nervous action which persist while the individual subject is quite unaware of them are to be declared as "mental" phenomena, the very notion of the unconscious mind will "pass into nothingness." Even apart from its usage in the newly formulated hypothesis of the unconscious mind the meaning of the term "unconscious," as often applied to actions and thoughts and desires by many speakers and writers, is generally vague and mostly misleading. The psycho-analytic schools, however, treat the "unconscious" as if it were a recognized and definite compartment of a somewhat indefinite whole called *Mind*, and apparently hold that in this compartment are retained in potential or actual activity all the impressions that have been instinctively experienced or otherwise *learnt* during an individual life from its outset. Many of such memories, as all must agree, can be instantly recalled on receipt of the appropriate stimulus; but many others, and especially such as are related to instinctive desires and have unpleasant associations, are held, on the hypothesis in question, to be preserved and active in the unconscious mind, having been purposively or otherwise repressed thither by the conscious mind. In view of the indefinite nature of what may be implied in the term *consciousness*—that "vague and treacherous word," as some psychologist has styled it—it appears that the basic principle of the methods of psycho-analysis is a highly fanciful and unverified assumption of a vast region of the mind, the most important contents of which are consciously—or unconsciously—repressed and purposive activities, frequently or constantly struggling, in the case of large numbers of persons, to escape from this repression which they suffer from the counter-activity of the conscious mind, or of some special factor of it assumed to exist, and to be delegated to carry out the repressive function while the whole mind's personal proprietor is quite unaware of the process.

This is, of course, but a very scanty outline of the hypothetical system on which the practice of psycho-analysis is founded, but it may serve to indicate the point of the allegation that the teaching of the new psycho-analytics does not satisfy any of the requirements of scientific investigation. The home of this school, indeed, seems to be much in the clouds, and its philosophers, like the Socrates of Aristophanes, to be "walking on air" while they "contemplate the sun."

But quite apart from this important question as to whether there is any scientific basis for the Freudian doctrines it must be recognized that the spreading employment of the now popular therapeutic methods arising from those doctrines is liable to produce, and actually does produce, multiform harm to many sufferers from various kinds of mental or nervous disorder. Doubtless some patients are benefited or may recover under treatment by psycho-analysts; so also do many who are treated by those who analyse (in the pre-Freudian sense) the cases of mental disorder which come before them, whether without knowledge, or with knowledge and general disapproval, of the Freudian doctrines. It is indisputable that minute and careful inquiry into the previous individual histories of all that large group, commonly called "functional" or "nervous" cases, has, for long, been made by thoughtful and experienced physicians, whether mental specialists or not, nor is it doubtful that there is a considerable field worked in common by some of the new psycho-analysts and the large group just indicated who ignore, or reject, the conception of the "unconscious mind" as set forth in the new psychology.

Since the main intention of the author of this book is to advocate the wide employment of the Freudian psycho-analysis in the medical investigation of criminals generally, the consideration of a few points mentioned by him seems to be of importance and to require short comments.

1. In the last three paragraphs of Chapter IV, "On the offender's unconscious mind," Dr. Hamblin Smith writes:

> "And what is the conclusion of the matter? . . . It is summed up in the saying that to understand all is to pardon all: the author does not mean that nothing is to be done to delinquents. He considers them worthy of the most careful treatment. . . . It is not meant that they" (that is, any officials of the law or others appointed in connexion with institutions) "are to make the necessary investigations. The Court must have the ultimate responsibility of dealing with the case. But it must employ experts in making the investigations."

It is clearly intended to imply that such experts must be chosen from among "psycho-analysts" only. Therefore further comment is needless on this extraordinary proposal to employ only one section of the medical profession to serve the State in this matter. Who is to direct the State authorities in this important matter of its choice of doctors?

2. On page 74 it is stated that "psycho-analysis is a science consisting in the investigation of the mode of working of the unconscious mind," and on page 79 we read that "nothing has to be more carefully avoided in psycho-analysis than any trace of suggestion by the psycho-analyst." This precaution is one on which there may or not be general agreement even among psycho-analysts, but it is to be gravely doubted whether the advice is likely to be generally followed in this form of practice.

3. The possible, or even probable, risk during the process of psycho-analysis of the transference of the patient's feelings towards other persons (whatever the feelings may be) to the psycho-analyst himself is strongly emphasized by the author.

> "It will be seen," he writes, "that psycho-analysis is a method of great difficulty, requiring knowledge of a special technique, much experience, and perhaps certain gifts which are not possessed by all. It is a trying process for the psycho-analyst; until an attempt has been made no one can conceive what a severe strain this method is."

This warning by Dr. Hamblin Smith doubtless comes from one who is unbiased by any consideration other than a desire to advocate the best method of investigation into the mental workings of offenders sent to him by courts of law, and whose evidently earnest belief is that psycho-analysis is the best method. One reflection following on the reading of these words of his is that only a very small proportion of men or women doctors could possibly be expected to combine all the qualities necessary to practise psycho-analysis properly, even were its soundness as based on science, and its successful application in practice, to be generally admitted. Several other comments suggest themselves on some of the actual results of this practice, but space forbids further enlargement on this particular point.

4. There is much significance in what the author says about the frequent resistance made by the subjects of psycho-analysis and the necessity for such persons to be frankly willing for the investigation to be made.

> "There is a form," he says, "of unconscious resistance, more common among intelligent patients. Some psycho-analysts think that intelligent subjects are the best to deal with, and that lack of intelligence is a great handicap to the method. If this opinion be correct it will limit the application of psycho-analysis to court work."

The author, however, states that he has had "some success in dealing with subjects who are far from intelligent," but he gives no details.

In his last short chapter, "Conclusions," the author faces the above-mentioned and other difficulties, and sketches a preliminary scheme for introducing the method of psycho-analysis into the English prisons, recommending that at first the effort should be limited. But although he regards it as doubtful whether any offender should be placed by a court even on "probation" without the most thorough examination, he suggests that a beginning might be made only with: (1) young offenders; (2) those who repeatedly commit the same kind of offence, especially when the motive is not apparent; (3) cases in which there is any other marked peculiarity about the offence. But this condition is extremely wide, for it must be remembered that of the large numbers of thieves, burglars, persons who obtain money on false pretences, and so on, nearly all confine themselves to one special line of offence only. The motive for this specialization is in most cases sufficiently apparent, and gives no occasion for raising any psychological problem: the criminal, like other

men, recognizes that practice in his craft, as in others, leads to perfection.

There are parts of this book well worthy of study by prison administrators and reformers, apart from the special matters already noticed. In the second chapter especially, where Dr. Hamblin Smith deals with the subject of the "Offender's conscious mind," there is much that deserves attention, and especially his thoughtful comments on the various test methods devised for arriving at a normal standard of intelligence for the purpose of comparison with the intelligence of persons whose mental power is under investigation.

Both professional and lay readers of the book who may be already acquainted with some of the many works on psycho-analysis which are issued frequently from the press will accord to the author their recognition of the high degree of clarity in expression and logical consistence that mark his writing, qualities not readily detectable in most publications by adherents of this school.

H. BRYAN DONKIN.

FEEDING IN INFANCY AND CHILDHOOD.

THE fourth edition of Dr. ERIC PRITCHARD'S *Physiological Feeding of Infants and Children*[2] is a much larger book than its predecessor. The new edition will be welcomed, and deserves a high place among British textbooks devoted to this difficult and very controversial subject. Dr. Pritchard has given much study to the theoretical side of the subject, and has had a very extensive experience in the practical side; his opinions therefore have weight and authority. It does not at all detract from that authority that he frankly confesses in his preface that he has changed his views in some important respects; he now advocates feeding from the first day of life, at intervals of three hours, and opposes also the doctrine that as the artificially fed infant grows older its milk mixture should be made stronger.

The title of the book fairly indicates its scope—the proper food for infants and children up to puberty, both in health and sickness, and the guidance of dietetics throughout this period by physiological teaching. The greater part of the book deals with infants, and the physiological standards here are human milk and maternal nursing. After setting out the physiological laws of breast-feeding, Dr. Pritchard lays down the main principles which should govern the artificial feeding of infants. The total daily energy value of the food taken must be known, and must correspond to the output of energy; the ratio of the organic constituents in the milk mixture must roughly approximate to that in human milk; accessory factors in the diet, such as vitamins, salts, and lecithin, must not be omitted; the importance of training the digestive organs of the infant to a fuller capacity must be kept in view. The illustration and application of these main principles run throughout the book, and it is by his insistence and reliance on principles that the author is able to give clearness and cohesion to his exposition of a complicated subject. He will, perhaps, not expect that all his doctrines, theoretical and applied, will be accepted by the critics; but he may be assured that they have the great and not too common merit of being readily understood. It is a great point with Dr. Pritchard that the energy output of the baby should be roughly measured and allowed for in planning his diet; that, for example, a lively, vigorous baby should be given a larger ration than a quiet and passive one; also that in wasted infants heat and energy should be conserved by warm clothing. He also strongly recommends the daily use of a vegetable and bone soup (for which a recipe is given) in order to supply salts, extractives, lecithin, and cholesterin; in addition to this, he advises the daily use of orange-juice, of some animal fat, and even of yeast preparations. He favours the use of barley water, and even of dextrinized flour in small amount, after the third month; and, after the sixth month, of some farinaceous food, to replace an equivalent amount of sugar. On all these and many other important, and often disputed, points in the dieting of infants and children Dr. Pritchard offers clear and reasoned opinions drawn from his own experience and study. Further experience and fresh discussion may change or confirm these opinions, but meantime, as presented in this book, they are an authoritative contribution to the subject.

[2] *The Physiological Feeding of Infants and Children.* By Eric Pritchard, M.A., M.D.Oxon., M.R.C.P.Lond. Fourth edition, entirely rewritten and enlarged. London: Henry Kimpton. 1922. (Roy. 8vo, pp. xvi + 500; 90 figures. 21s. net.)

DURATION OF FATAL LUNG TUBERCULOSIS.

THE *Clinical Course and Duration of Fatal Lung Tuberculosis*[3] is an unpretentious little book compiled by Dr. C. H. WÜRTZEN from statistics collected over a period of nearly fourteen years at the Oeresund Hospital, Copenhagen. In order to avoid the fallacies inherent in all methods dependent upon the following-up system, he has confined himself to the consideration of those patients who actually died during their stay in hospital. In this way he had before him data referring to 1,032 men, 780 women, and 87 children, nearly all of whom belonged to a more or less homogeneous class of insured people working in the city. Dating the onset of the trouble from the first manifestation of symptoms, adding together the number of months elapsing in each case before death, and dividing by the total number of patients, he has obtained a figure which represents the mean duration of the disease. For men this works out at 37.1 months, for women at 34.4 months, and for children at 11.9 months. Further, by subdividing each class into age and sex groups, he has shown that though the preponderating incidence of phthisis falls amongst young adults, the greatest fatality occurs in childhood and old age. An initial haemoptysis appears to be a favourable sign, while complications such as diabetes and syphilis increase the gravity of the prognosis. Limited as the book is in its scope, the data themselves are of considerable interest.

PUBLIC HEALTH CHEMISTRY.

The Chemical Examination of Water, Sewage, Foods, and Other Substances[4] is the title of a book written by J. E. PURVIS and T. R. HODGSON for those who perform laboratory investigations for public health purposes; it deals also with a number of other matters of a kind commonly submitted as subjects of inquiry to analysts. The first chapter describes methods for determination of the dissolved constituents of water and sewage, and gives the results of analytical examination of a number of samples; analytical methods applicable to works effluents are also noticed. In the second chapter milk, cream, dried milk, and condensed milk are dealt with on a similar plan. Succeeding chapters relate to oils, edible fats, beverages, cereals, spices, and other articles of diet. One chapter is devoted to the recognition of poisonous metals in foods, another to toxicological analysis. Air, coal gas, rag flock, and the examination of urine are included among the miscellaneous subjects.

The text consists chiefly of methods which are well known to experienced analysts and which are described, often with greater detail, in other works; a certain number, however, are based on principles differing from those of the older type. There is no remarkable departure from the plan of other books of its kind and no fault is to be found with the quality of the matter—indeed the information given is presented tersely and without ambiguity; but anyone looking for the help that will lift him above the difficulties inherent in analytical practice will be disappointed. There is a growing disposition to give directions in the terms that might appropriately be used to a chemical factory hand, and to omit reference to the highly important principles of theoretical chemistry involved in the instruction. Such directions are suited only for routine work; those who have to deal with the same problems complicated by unusual conditions are obliged to seek refinements in methods of procedure and prefer to receive directions couched in the language which one chemist would use to another. What the authors have done in this direction is only sufficient to make prominent the need for more chemistry in the discussion of technology. The collection in a handy form of much that is required for public health work renders the volume quite suitable for those engaged in that practice. It contains some interesting descriptions of the authors' own results in the analyses of sewage products and other matters.

The fact that the work has reached its second edition in a brief period is proof that it has met with appreciation; it can be recommended to those who already possess treatises on its subject, since some of the methods of procedure offer advantageous alternatives to the older methods of practice.

[3] *A Contribution to our Knowledge of the Clinical Course and Duration of Fatal Lung Tuberculosis.* By Dr. C. H. Würtzen. London: Gyldendal. 1922. (Med. 8vo, pp. 43. 2s. 6d. net.)

[4] *Chemical Examination of Water, Sewage, Foods, and Other Substances.* By J. E. Purvis, M.A., and T. R. Hodgson, M.A. Second and enlarged edition. Cambridge: The University Press. 1922. (Demy 8vo, pp. 346. 20s. net.)

NOTES ON BOOKS.

THAT a second edition of TIDY'S *Synopsis of Medicine*[5] should be called for within sixteen months of the publication of the first proves that it is popular and has realized the objects intended by the author. The book is not meant to take the place of the larger treatises of medicine, but by its compactness, its accuracy in detail, and its clearness of arrangement will appeal to the student reading for an examination and to the examiner himself. The new edition does not differ substantially from the first; a few minor mistakes have been corrected and the section on encephalitis lethargica has been rewritten. Had a fuller revision been considered desirable we might have hoped for more on the subject of the pathogenesis of gastric ulcer, which is barely touched on. We note also that Vincent's angina has been omitted and are somewhat surprised to find that in the section on asthma no space has been allotted to the discussion of the relation of that disease to hypersensitiveness, whereas in the section on the nervous system perhaps too much space has been given to such conditions as myotonia congenita, paramyoclonus multiplex, and amaurotic family idiocy. Otherwise we have nothing but praise for the book; impartial consideration has been given to all views of any importance, and the information provided is nearly always comprehensive and up to date. A word of praise is due also to the skilful way in which Dr. Letheby Tidy has dealt with the treatment of each particular disease; for this reason alone the book is of great value for reference in a difficulty, and it has a good index.

The modern nurse is expected to absorb so much science in the course of her training that it is sometimes urged against her by her critics that the pursuit of knowledge leaves her no time to cultivate that sympathetic attitude which means so much to the helpless patient. There should be no room for any such criticism in the case of anyone who takes as her textbook Miss BERTHA HARMER'S *Text-book of the Principles and Practice of Nursing*.[6] In the course of the introduction Miss Harmer sets out in clear and simple language the spirit and ideals of the nursing profession and those qualities which every nurse should strive to cultivate. Something deeper than sympathy, kindness, and unselfishness is called for in the perfect nurse, and can only be attained by a wide professional knowledge, assisted by the priceless gift of understanding which brings not only comfort to the body but ease and rest to the mind of the sufferer. Miss Harmer never allows the reader to regard the patient merely as a subject upon whose body certain rites have to be performed; the patient is always a sensitive human being whose feelings are to be respected. The first half of the book covers the general principles of elementary nursing, the second part being devoted to a more detailed account of the technique of medical and surgical nursing. There is also a section on the care of eye, ear, nose, and throat cases. In each instance the underlying principles are lucidly explained, so that the student can adapt the teaching to meet any conditions, whether in a private house or in hospital. The various methods and procedures are very fully described, and no pains have been spared to make every detail perfectly clear. The illustrations have been well chosen, and the publishers are to be congratulated on the excellence of their execution. This book is a mine of information for the probationer who is preparing for her examinations; it should prove of equal value to the fully qualified nurse, and should be of great assistance to those responsible for the teaching of the coming generation of nurses.

The report[7] of the Conference on Mental Deficiency, held at the Caxton Hall, Westminster, on July 26th and 27th (of which an account appeared in the JOURNAL of August 5th, 1922, p. 222), has been published by the Central Association for Mental Welfare, and copies may be obtained from the honorary secretary of the association, Miss Evelyn Fox, 24, Buckingham Palace Road, S.W.1. The report contains papers on "Crime and mental deficiency," by Sir Bryan Donkin, on "Criminal defectives," by Dr. W. Norwood East, and on "Economic difficulties which prohibit the development of special schools," by Dr. H. B. Brackenbury, with speeches by Sir Leslie Scott, Mr. H. A. L. Fisher, and others, and a full account of the interesting discussion which took place.

[5] *A Synopsis of Medicine.* By Henry Letheby Tidy, M.A., M.D., B.Ch.Oxon., F.R.C.P.Lond. Second edition, revised. Bristol: John Wright and Sons, Ltd.; London: Simpkin, Marshall, Hamilton, Kent and Co., Ltd.; Toronto: The Macmillan Company of Canada, Ltd. 1922. (Cr. 8vo, pp. xv + 956. 21s. net.)

[6] *Text-book of the Principles and Practice of Nursing.* By Bertha Harmer, B.Sc. Columbia Univ., R.N. New York: The Macmillan Company. 1922. (Demy 8vo, pp. xiv + 695; 153 figures. 14s. net.)

[7] *Report of a Conference on Mental Deficiency.* To be obtained from Miss Evelyn Fox, 24, Buckingham Palace Road, S.W.1. Price 3s.

SIGHT-TESTING BY OPTICIANS.

REPORT BY THE COUNCIL OF BRITISH OPHTHALMOLOGISTS.

THE following report on sight-testing by opticians has been issued by the Council of British Ophthalmologists, and will appear in the *British Journal of Ophthalmology*. We are indebted to the Honorary Secretary for an early copy.

In 1906, and again in 1919, opticians have made application to the Legislature that their craft may be legally recognized for the purpose of sight-testing, and it is consequent upon these efforts that the Council of British Ophthalmologists has thought it desirable to consider the matter in the interests of the general public.

Training of Opticians.

The Council would warmly welcome any scheme which would lead to greater efficiency in the making and fitting of spectacles. It fully recognizes that there is a very definite need for a greater supply of properly trained opticians, and ophthalmic surgeons often have cause to deplore the inefficiency displayed in carrying out their prescriptions for glasses.

Sight-testing by Opticians.

In a recent petition (1919) the British Optical Association claimed that opticians should be recognized as capable, not only of carrying out the optician's art of making and fitting glasses in conformity with prescriptions, but also of measuring and determining what glasses are required to compensate for defects of vision in any member of the public who may apply to them. Paragraph 10 of the petition stated:

"In a very large majority of refraction cases which can be treated by glasses, members of the public do, in fact, visit an optician rather than an ophthalmic surgeon or medical man, and the association humbly submit that it is eminently in the public interest that the optician should be a skilled man and under suitable supervision. A qualified optician, especially when holding a Fellowship Certificate of the Association, would recognize a case in which the eye, through disease or otherwise, could not be properly treated by glasses, and would direct the patient to an ophthalmic surgeon or medical man. An ignorant optician would be likely to supply the patient with glasses which might do great harm."

Training Necessary for Sight-testing.

The Council, however, considers that no course of training short of that required for full medical qualification can produce the skill and judgement necessary to secure the requirements stated in the above paragraph. Every medical man dealing with ophthalmic cases must be equipped with the knowledge necessary for ordinary qualification in medicine, and, in addition, with special knowledge of the most delicate and complex sense organ in the body.

It is the opinion of the Council that any State recognition of sight-testing by persons possessing only an optical qualification would not be in the interests of the community.

The Scientific Principles of Sight-testing.

The art of prescribing glasses can be divided into two periods—the purely empirical period preceding 1850, when only subjective methods of testing were available, and the period following 1850, when accurate objective measurements began to be used. (See Appendix.) Those scientific methods have been developed by medical research, and to a great extent they are not available to the optician. The statement that where defective vision is due to other than optical conditions it should be treated by a duly qualified medical practitioner (see petition of the British Optical Association, par. 10, quoted above) is in itself sufficient argument against the optician's claim, since it is well known that changes in the refraction of the eye are often produced in the early stages of serious eye disease. In many such cases an optician may be successful in raising the acuteness of vision to a normal standard, but he would almost inevitably fail to recognize the disease which is the cause of the refractive error. In fact, disease very serious to the eye, or threatening even life, may occur in an eye with perfect acuity of central vision.

Use of Drugs.

An adequate examination of the eyes and a correct determination of the error of refraction cannot be made in young children, especially in cases of squint, while the accommodation (that is, focusing power) is active. The absence of accommodative effort can only be ensured by the use of certain drugs, which also dilate the pupil. These drugs

must not be used in an indiscriminate manner. In certain conditions of the eye their employment is attended by grave risk to sight. In some individuals they produce serious constitutional disturbances. As dilators of the pupil their use is frequently essential in order to determine the presence or absence of changes in the retina or optic nerve. Such changes may be the first indication of general disease, by the prompt treatment of which the life of the patient may be saved or prolonged.

Eye Defects and General Disease.

The treatment of headaches, associated with errors of refraction, demands not only the use of glasses, but also constitutional treatment, which can only be determined by a medical man. In some cases of defects of the muscular balance of the eyes the use of prisms is necessary. The correct estimation of these and a complete investigation of the case are most difficult problems, since some of these muscular defects are among the earliest signs of serious diseases of the nervous system.

Changes in the refraction of the eyes are often produced in the early stages of eye disease. For example, myopia ("short sight") often appears in the early stages of cataract, or of chronic glaucoma, a disease which untreated inevitably leads to blindness. Hypermetropia ("long sight") may be met with in the early stages of a malignant tumour. In such cases glasses may bring visual acuity up to a normal standard, but an optician will fail to recognize the disease, which will thus be left to run its course.

Optical defects and disease constantly overlap; the former cannot be differentiated with certainty from the latter, nor the latter definitely excluded, by any, but a medical practitioner who has had special training and experience.

Optician's Standpoint.

The "sight-testing optician" endeavours either to supply spectacles with which the customer considers he can see to his liking, or to provide such lenses as will convert optically imperfect eyes into accurately focusing instruments. All are agreed that the former procedure is indefensible: the latter needs further consideration.

The eye is an integral part of the human body. Developmentally it is, in its most essential elements, an offshoot of the brain. There is practically no organ of the body which does not react upon it to its advantage or its detriment. Without exposing it to the gravest misfortune it cannot be dealt with as an inert, isolated optical instrument, yet it is in this way only that the optician can view it, and in this way only can he adapt mechanical apparatus to such of its optical defects as his limited means may enable him to recognize. Without the use of drugs to dilate the pupil or paralyse the focusing muscle, in many cases he cannot measure accurately the error of refraction or be in a position to identify the cases which demand medical advice and treatment. If he were allowed to use such drugs he would become an even greater danger to the community by reason of serious disease which he in his ignorance might produce.

Ophthalmic Surgeon's Standpoint.

The ophthalmic surgeon approaches his refraction work from an entirely different standpoint. To him the eye is an optical instrument, but it is also an integral part of the human body in complex interrelation with the other parts. Its anatomical proportions and its physiological activities are before his mind. Its pathological disturbances, both local and those dependent on general disease, are known to him. He has at his disposal the use of all drugs necessary for his purposes, and of the indications for and against their employment he is fully aware.

In the investigation of diseases of the eye, the measurement of the acuteness of vision, both with and without lenses, is one of the first steps in the examination of the patient. In refraction work the surgeon takes into consideration the physiological activities of the normal eye. The hypermetropic eye he regards as developmentally imperfect. Astigmatism may be due either to developmental malformation or to disease. Presbyopia (loss of focusing power associated with advancing age) is a physiological condition, but undue rapidity in its progress may herald glaucoma, and apparent recovery of focusing power may indicate the earliest stage of cataract. Myopia is in many instances pathological, and the myopic eye is exposed to grave disorders. With a comprehensive knowledge of facts such as these, the ophthalmic surgeon decides in a pure refraction case what lenses should be prescribed. With what lens the patient sees best is only one point he takes into consideration when prescribing. His aim is not only to improve vision, but also to secure the health and comfort of the patient. No case is dismissed until full ophthalmoscopic and other examination has excluded all objective signs of disorder.

If disease be present, its causation, whether local or general, has to be ascertained, and this demands a knowledge of the diseases of the other organs of the body which produce changes in the eye. The ophthalmic surgeon must have an adequate knowledge of diseases of the brain and central nervous system, of the blood vessels and vascular system, of the kidneys, of the nose and its accessory sinuses, of the various ductless glands, etc. In fact, there is no branch of medicine which is not in close relationship with this special domain, nor is there any specialty in which a general medical knowledge is of greater importance.

The Public Interest.

It cannot be in the interests of the community to allow such grave responsibilities to pass into the hands of men with no medical training, and to hall-mark by official recognition a practice involving such dangers.

Many people in the past have gone to opticians to obtain glasses for failing vision under the impression that they are fully qualified to prescribe. Official recognition of sight-testing opticians would encourage the practice and would increase the feeling of security which our arguments show to be unwarranted. There can be little doubt that this impression has been fostered by such "qualifications" as F.S.M.C., F.B.O.A. (Fellowship of the Spectacle-makers' Company, Fellowship of the British Optical Association), etc. It is the duty of the State to guard against legislation which may in any way entail detriment to the community.

APPENDIX.—HISTORICAL.

An inquiry into the history of the science and art of refraction will show that this branch of ophthalmic work has been initiated and developed by medical men, and that even at the present day the optician works, and must of necessity work, largely on the more purely empirical lines of the early part of the nineteenth century.

The discovery of spectacles as an aid to vision dates from the thirteenth century. There is no absolute certainty as to their first inventor, but the probabilities point to Roger Bacon (1214-1294), who, in his "Opus Majus," wrote of the enlarging power of a plano convex glass and of its value "senibus et habentibus oculos debiles." Either directly from Bacon, or from some other monk, the discovery became known in Italy, and at the end of the thirteenth century spectacles were being made by Alessandro de Spina, a Dominican friar of Pisa. He did not claim to be the actual inventor, but had seen glasses made by someone else who was unwilling to reveal the secret. It may have been from Salvino d'Armato, of Florence, that Spina obtained the secret, since Armato's tombstone bears the inscription: "Here lies Salvino d'Armato degl' Armati of Florence, inventor of spectacles. God forgive him. Anno D. 1317."

If Roger Bacon invented spectacles it was probably some time before the year 1267, when the "Opus Majus" was written for Pope Clement IV. By the middle of the fourteenth century convex glasses had become fairly common. Concave glasses seem to have come into use first in the sixteenth century, and early in the seventeenth century Kepler wrote the first important scientific work on the use of spherical lenses.

The next important discovery did not take place till the beginning of the nineteenth century, when Thomas Young, the distinguished physician and physicist, in his "Memoir on the mechanism of the eye" (*Phil. Trans. Roy. Soc.*, 1801), gave the first description and measurement of astigmatism and a table of optical constants in close agreement with modern determination. He had previously (1793) written a paper on the mechanism of accommodation which secured his election to the Fellowship of the Royal Society. His observations were subsequently confirmed by Airy in 1823, but remained practically unknown to opticians.

Until the year 1853 the prescribing of spectacles was entirely empirical. It was known that men, as they reached middle life, had difficulty in seeing to read, and that their difficulty was relieved by wearing suitable convex glasses. It was occasionally found that younger people also were helped in reading by the use of convex glasses, and they were said to have "oldsight," a phrase still to be heard in use amongst opticians. Another group of people was said to have "weak sight," and it was found that they were enabled to see more clearly in the distance by the use of concave glasses. The sale of spectacles was often in the hands of country pedlars, and people chose from the stock what seemed to suit them best.

With the discovery by Helmholtz of the ophthalmoscope and the ophthalmometer in 1853, the scientific investigation of the refractive media of the eye became possible and the work of Donders, the great Dutch surgeon, speedily laid the foundations on which all modern refraction work is built. He showed the way in which a hypermetropic eye and a myopic eye depart from the normal, and the liability to disease existing in a myopic eye. He showed the relationship between the long-sighted eye and squint, and the essential difference between long sight and old sight. He discovered the frequency of astigmatism and laid down the rules for

its detection and estimation, and showed how to determine the strength and position of the cylindrical glasses necessary for its correction. Donders also established a standard for normal vision, and for the first time rendered accurate "sight testing" possible. He reconstructed the scale of lenses, substituting the metre for the inch as the unit of measurement.

This work has been continued and extended, corrected and amplified, but the progress has been entirely due to the work of medical men. In 1873 Cuignet, a French military surgeon, discovered an additional method of measuring the refractive condition of an eye, which rendered the ophthalmic surgeon still less dependent on the subjective methods previously in use. By the method of retinoscopy the skilled ophthalmic surgeon is enabled to make accurate measurements of the static error of refraction. These measurements can only be accurate in the absence of any accommodative effort on the part of the patient under examination. This condition of absence of accommodative effort can only be ensured by the use of drugs which paralyse the ciliary muscles. At a later date the use of prismatic glasses was introduced by medical men to alleviate symptoms due to errors in the muscular balance of the two eyes, and the determination of the conditions under which prisms should be ordered is one of the most difficult problems an ophthalmic surgeon has to solve. It involves the knowledge, not only of the inborn defects of musculature, but also of acquired defects, and of the pathological causes which may produce them.

Nova et Vetera.

THE INTRODUCTION OF ETHER ANAESTHESIA.

If we exclude early experiments with nitrous oxide gas the first vapour or gas to be used for the purpose of producing general anaesthesia was ether. The story of its introduction by William Morton, a dentist, was told at considerable length in an article on the Jubilee of Anaesthesia published in this JOURNAL on October 17th, 1896. It was written by the late Mr. C. Louis Taylor, then Assistant Editor of this JOURNAL, and the substantial accuracy of the story has not been called in question. But some confusion has been introduced owing to the fact that Morton had used ether in private before it was used in public. The use of ether had been suggested to Morton by Dr. Charles T. Jackson of Boston, a distinguished chemist whose pupil he had been. Morton proceeded to make some experiments on himself, and finally on a patient who had gone to his surgery to have a bicuspid tooth extracted. The ether was given on a handkerchief, but it seems clear that general anaesthesia was produced. The first operation in public under ether was performed by Dr. John C. Warren, senior surgeon to the Massachusetts General Hospital, on October 16th, 1846; it was for congenital vascular tumour of the neck in a young man. General anaesthesia was produced; after the operation Dr. Warren, turning to the audience, said in an impressive tone, "Gentlemen, this is no humbug."

We are indebted to Dr. H. C. Crouch of Ascot for a copy of the following letter he has received from Dr. W. W. Keen, who has lately celebrated his eighty-sixth birthday:

1520, Spruce Street,
Philadelphia,
October 6th, 1922.

Dear Doctor Crouch,

In reading your article on anaesthesia in the eleventh edition of the *Encyclopaedia Britannica* I was much struck by the fact that you gave prominence to the operation done under ether on September 8th, 1846, but did not mention the operation of October 16th, 1846.

The operation on September 8th was a private affair in the office of Dr. Morton. It was not witnessed by any number of people; it was not made public; it made no impression on the local community or on the world at large.

I am sending you, under separate cover, a pamphlet by Professor Welch of Johns Hopkins University (whom you know, of course, by name) which enters into the whole question of the introduction of surgical anaesthesia in a most candid and critical spirit. At the same time it gives the actual facts which attended and followed that notable operation of October 16th, 1846. This operation was done in the presence of the medical class of Harvard University, of a large number of physicians of the city of Boston, of the surgeons of the hospital themselves, and immediately was flashed round the world, by mail in those days of course. It aroused at once the deepest interest in England, and, to state the result in a word, it was the single starting point for the wide dissemination of the fact of surgical anaesthesia.

Moreover, it was the origin of the whole nomenclature relating to it. Prior to October 16th, 1846, the words anaesthesia, anaesthetic, anaesthetist, etc., were not in existence. They were happily coined by Oliver Wendell Holmes, the Professor of Anatomy at Harvard, and who was distinguished the world over for his later literary work. You will observe, therefore, that from the point of view of publicity, of importance, and of initiative, that date stands out conspicuously.

I wrote to the editors of the *Encyclopaedia*, in this country, asking them to transmit to the central office in London, and to the author, yourself, a letter calling attention to the inadequate—or I ought rather to say incorrect—statement in this article, incorrect by omission.

May I also add a delightful witticism of Dr. Holmes? When it was proposed to put up a monument to the discoverer of ether in the public gardens of Boston, where the monument now stands to-day, immediately a great contest arose as to whether Morton's name or Jackson's name should be inscribed on the monument. Naturally they came to Holmes for a solution of this difficulty. With his ready wit he replied at once, "Nothing is easier; put up your shaft with a bust of Morton on one side and of Jackson on the other, and between them 'To ether.'"

Of course, the witticism would be lost very much by the pronunciation of "either" as if it were spelled "eyether." In those days the almost universal pronunciation in America was "eether." Of late years the English pronunciation of the long "i" in the first syllable has grown into considerable use, though still yet, I think, not the prevalent one in the United States.

Yours very truly,
W. W. KEEN,
Hon. F.R.C.S.,
Eng., Edin., and Ireland.

In a letter dated Boston, April 2nd, 1893, Dr. Oliver Wendell Holmes, who in 1846 was Professor of Anatomy at Harvard, wrote:

"The discovery was formally introduced to the scientific world in a paper read before the American Academy of Arts and Sciences by Dr. Henry J. Bigelow, one of the first, if not the first of American surgeons. . . . He had taken a great interest in the alleged discovery, had been present at the first capital operation under its influence, and was from the first the adviser and supporter of Dr. W. T. G. Morton, who had induced the surgeons of the hospital to make trial of the means by which he proposed to work this new miracle. The discovery went all over the world like a conflagration."

It reached London within about two months, the flame being carried in a letter from Dr. Bigelow to Dr. Boot of Gower Street, who immediately communicated the facts to Mr. Liston, then surgeon to University College Hospital. Liston consulted a friend, Mr. Peter Squire, a well-known pharmacist. It so happened that Mr. Squire had a nephew (afterwards Dr. William Squire) who had entered University College that October, and that this young man had made some experiments on himself with ether in the chemistry class at the College and had found out that he could bruise his knuckles across the iron ends of the classroom desks without any sense of pain at the time. Young Squire rigged up an apparatus with a glass bottle and inhaled ether in Liston's presence. Liston made a small puncture under Squire's finger-nail and was satisfied that he was insensible to pain. Liston had at that time under his care a delicate fair-haired man worn out by suppurating disease of the knee and loss of sleep from the jerks caused by eroded cartilage. On December 21st Squire administered ether to this patient and Liston amputated above the knee. Liston was famous for his speed, and the amputation was completed in twenty-seven seconds. The patient was quite unconscious during the operation, and so remained when removed from the theatre. Dr. F. William Cock gave many details of the occasion in the *University College Hospital Magazine* in 1911. He had consulted the notes made in the case book at the time and had conversed with three persons who were present—the late Dr. Frederick Cock (Dr. William Cock's father), his brother-in-law, Dr. Henry Maund, and Dr. William Squire, whose name has already been mentioned. It may be remembered that it was announced at the recent annual dinner of past and present students of University College Hospital that Dr. William Cock had had two chairman bells made to commemorate the first operations under ether in America and in this country. He presented one of the bells to the Massachusetts General Hospital, where the first operation under ether was performed, and the other to University College Hospital. The bells are made from the metal of an old bell in the church of Appledore in Kent (1621), and each is supported on an iron hoop made from the rails of the surgical theatre in the old University College Hospital. The stand is made from the oak frame of the old bells at Appledore (1685). Each bell bears the same inscription round the crown, NOLAE PULSATIO AMORIS RATIO. On one side is "Genl. Hosp. Mass. Oct. 16th," on the other "Univ. Coll. Hospl. London. Dec. 21st," and, in the middle, the year—1846. In explanation of the inscription round the crown it may be said that Nola in Campagna was the chief place for bell-founding in the early times, so that its name became synonymous with bell. The inscription may be freely translated "When I do sound let joy abound."

British Medical Journal.

SATURDAY, DECEMBER 2ND, 1922.

STANDARDIZATION OF PITUITARY EXTRACT.

THE first of the reports of the Medical Research Council on "biological standards"* deals with the methods available for the standardization of pituitary extract, and gives an account of experiments carried out by Dr. J. H. Burn and Dr. H. H. Dale with a view to establishing a more accurate method of estimating the activity of this substance. Extracts of the pituitary gland are widely used in medical and surgical practice, yet up to the present very little attempt has been made by different manufacturers to provide extracts of similar potency. Some system of standardization is all the more necessary because this remedy is often used in emergencies—as, for example, in the difficulties and accidents of childbirth—and on such occasions it is all-important that the correct dose should be administered. Pituitary extract, a remedy of great value when accurately used, may, when inaccurately employed, produce dangerous and even fatal consequences. Obviously the physician should know the strength of the preparation he intends to administer, yet the experiments described in this report show that commercial preparations may vary so greatly that the most potent may have eighty times the strength of the least potent. Thus a doctor, having become thoroughly familiar with the activity of one preparation, may, when employing another which is apparently equivalent, inadvertently administer eighty times the intended dose. This absence of uniformity in the strength of different preparations is not necessarily the fault of the manufacturers, since no official guidance has in this country been given to them as to the strength of the extract most suitable for therapeutic purposes, and there has been no standard of activity available for common use by which fresh extracts can be judged. The authors of this report describe a method by which a preparation of uniform activity can be made and used for purposes of reference, and recommend the adoption of a definite standard of potency in the *British Pharmacopoeia*. The absence of official standards of value and authenticity for drugs of this kind and for the numerous biological preparations, such as serums and the like, used in general practice, has already been publicly denounced as "discreditable to our national position in the world of science and a source of grave danger to the community."

Burn and Dale point out in the report that the active principles of the posterior lobe of the pituitary body are unknown, so that the only method of estimating their presence is the physiological. A watery extract is very unstable. The active principles are easily destroyed in the process of preparing the extract, so that the first essential is some standard with which all preparations can be compared. The therapeutic properties of pituitary extract depend on at least two principles, one acting on the blood pressure and one on the uterus, and any method of standardizing must measure one or other of these activities accurately. Difficulties arise when the blood pressure is selected as the standard, owing to the fact that no great delicacy of discrimination can be secured in estimating the pressor activity of the gland, the total effect being dependent in all probability on the action of more than one pituitary principle. Moreover, recent work has shown that tolerance is rapidly established for the action of the most important pressor principle, a fact which further complicates attempts to estimate the value of the extract on the basis of its effect on blood pressure. On the other hand, tests made on the isolated uterus of the guinea-pig detect differences of activity within much narrower limits, and actually determine the particular form of activity which has given to the extract its widest use in therapeutics. The authors conclude that this test is by far the most suitable for quantitative comparisons with a standard, but that it should be supplemented occasionally by a test on the blood pressure to ascertain that the pressor activity is not disproportionately defective.

Full particulars of the method recommended are given in the report, but the essential details are as follows. The apparatus consists of a cylindrical glass testing vessel holding about 200 c.cm., set in a stout copper thermostat bath filled with water kept at 37° C., the testing vessel being so arranged that it can be emptied and refilled from a reservoir of warm saline. The uterus to be examined is fixed in the testing vessel, and the upper end attached to a lever which writes on a rotating drum. The fluid used in the testing vessel is a modification of the Locke-Ringer solution, differing in that it contains more sodium bicarbonate and a minute proportion of magnesium chloride, which has the useful effect of weakening the tendency to irregular spontaneous rhythm and preserving the excitability of the muscle to pituitary extract. Virgin guinea-pigs weighing between 200 and 300 grams are chosen for the experiments; when the uterus is "on heat" it is unsuitable, and the authors recommend that the young females should be segregated as soon as they are ready to leave the mother, and that the absence of oestral activity should be verified by external inspection before the animal is killed. The whole horn of the uterus should be used, suspended between a cervical tag at one end and the ovary at the other. The pituitary extract for the test is diluted 100 to 200 times with Ringer's solution, so that the dose to be added to the bath shall not be too small for reasonable accuracy of measurement, or so large that its addition unwarmed will sensibly affect the temperature of the solution in the testing vessel.

It would be a great advantage if a stable chemical substance could be prepared of known chemical composition which acted on the uterus in the same way as the pituitary extract, and which might be used as a standard with which the pituitary extract could be compared. Many experiments were carried out with histamine in the hope that it would fulfil these requirements, but the authors were led to the conclusion that the uteri from different guinea-pigs vary independently in their sensitiveness to histamine and to pituitary extract respectively, and these variations are such that histamine as a standard for pituitary extract is unsatisfactory. A similar disappointment attended attempts to use potassium chloride as a standard, for here again it was found that sensitiveness to potassium chloride did not run concurrently with sensitiveness to pituitary. No satisfactory artificial standard having been found, an extract made from the perfectly fresh pituitary gland was chosen as a standard. This extract must be prepared from glands received direct from the slaughterhouse as soon as possible after the ox has been killed. The posterior lobe is shelled out and divided up with small dissecting scissors and weighed, extracted with water in the proportion of 1 gram of gland to 40 c.cm. of water, raised rapidly to the temperature of boiling water and filtered. The filtrate represents 2.5 per cent. extract of the fresh gland substance.

In carrying out the test a fiftyfold dilution of the standard fresh extract is added to the testing vessel and the effect on the uterus recorded on the drum. The aim

*Reports on Biological Standards. I: Pituitary Extracts. Special Report Series No. 69. By J. H. Burn, M.A., M.B., and H. H. Dale, C.B.E., M.D., F.R.S. (1s. 6d. net.)

in every case is to establish for the particular preparation the dose, which is about 60 to 70 per cent. of that needed to produce contraction of the muscle to the maximum. When the standard dose is thus fixed the determination of the exactly equivalent dose of the preparation to be tested is made from another series of experiments.

There are many stages in the preparation of the standard extract where any departure from the method recommended will result in serious loss of activity, but the authors have shown that an extract of perfectly fresh infundibular material, prepared by a method kept exactly constant in all its details, furnishes a sufficiently constant standard of reference for the biological testing of pituitary extracts. It is, however, not possible to prepare the large quantities of pituitary extracts required to meet the present-day demands with all the precautions observed in the preparation of the standard extract, and local conditions and the different processes adopted by commercial firms are the causes of the widely differing potency of various extracts to which reference has already been made. Dale and Burn have compared three British and two American makes of the extracts on the English market with the standard extract previously described, and have found very marked variation both in the effect on the isolated uterus and in the pressor effect on blood pressure, although in each case the extracts were described by the manufacturers as "physiologically standardized." This variation is due to two different factors. In the first place, the proportion of gland substance in a given volume is not constant for different preparations. Several manufacturers have now abandoned the custom of stating the supposed strength of their extracts, and medical practitioners, finding two different preparations of the pituitary gland, both dispensed in sealed ampoules containing 1 c.cm., are naturally apt to assume that they are equivalent, or intended to be so. The *British Pharmacopoeia* has not yet recognized the existence of this remedy, but the United States *Pharmacopoeia* has officially settled the theoretical strength at 10 per cent. of the fresh infundibular substance. The report recommends the general adoption by British manufacturers of this theoretical standard, so that the practitioner may be justified in his assumption that the dose contained in the same volume is at least supposed to be the same, whatever preparation he uses.

In the second place the actual yield of activity obtained from the same weight of gland substance is widely different in the case of different preparations, owing to variations in the method of manufacture. Preparations as potent as the standard fresh extract cannot be produced on a commercial basis, but the report suggests that 60 per cent. of the activity of the standard extract is a level which should be attained without difficulty by any manufacturer who has the necessary equipment and staff for the careful extraction of fresh material which has been dried at low temperatures when perfectly fresh and used without unduly long storage. The standard should be freshly prepared as often as required, but it is not suggested that a new standard solution is necessary for the assay of every batch of commercial extract. A comparison of each batch with its predecessor would suffice for limited periods, reference being made to the independent standard at regular intervals.

Until some such uniformity has been achieved it will be impossible to arrive at any correct value for the dose of pituitary extract to be used in treatment. A committee appointed by the Obstetrical Section of the Royal Society of Medicine, with the co-operation of the Medical Research Council, is conducting a thorough investigation into the question of the doses appropriate to various conditions.

SUICIDE AND FELO DE SE.

OBSERVATIONS made from time to time by coroners show that there is still considerable misunderstanding as to the precise meaning of the words "suicide" and "*felo de se*," and of the effect of adding to a verdict the words "while temporarily insane" or "while of unsound mind." The general practice at inquests is to use the word "suicide" where the jury or coroner is of opinion that the deceased, through unsoundness of mind, was incapable of appreciating the distinction between right and wrong, and accordingly of committing a crime; the term "*felo de se*" being restricted to the very small proportion of cases in which the deceased was considered to have been of sound mind. This custom appears to have grown up among coroners without any legal sanction or guidance.

The whole question of terminology and legal effects in these cases was very thoroughly investigated by Mr. Henslowe Wellington, whose able paper on the subject will be found in Volume I of the *Transactions* of the Medico-Legal Society. In law, there is no distinction between suicide and *felo de se*. The word "suicide" does not seem to have been used in works on law previous to 1736, when it appears in Hales's *Pleas of the Crown*, edited by S. Emlyn sixty years after Hales's death. A long series of judicial decisions and opinions show conclusively that suicide means self-murder.

Sir James Fitzjames Stephen says in his *Digest of Criminal Law* (fifth edition, 1894) that "a person who kills himself in a manner which in the case of another person would amount to murder is guilty of murder, and every person who aids and abets any person in so killing himself is an accessory before the fact, or a principal in the second degree in such murder." It is for this reason that when two persons agree to commit suicide together and only one dies, the survivor can be indicted for murder. Suicide is accordingly the same as *felo de se*, and the use of one or the other term might well be discontinued. The verdict "suicide while of unsound mind" is a contradiction in terms, and from the legal point of view meaningless. Chief Baron Pollock stated in 1847, "in point of law, as soon as it is ascertained that a person has lost his sense of right or wrong (it matters not what else of the human faculties or capacities remain) he ceases to be a responsible agent, and in my judgement can no more commit suicide than he can commit murder." The Home Office Departmental Committee on Coroners in its report published in 1909 recommended that the verdict of *felo de se* should be abolished. It advised that in cases of suicide the verdict should simply be that the deceased died by his own hand (stating how), but the jury should be at liberty to add to their verdict that there was no evidence to show the state of his mind, or that at the time of taking his life he was of unsound mind.

It seems clear that the verdict "suicide" coupled with the words "while temporarily insane" came to be used by coroners' juries for the purpose of avoiding the degradations which were inflicted upon the corpse of the *felo de se*, and the penalties which his relatives suffered. Until 1823 it was the practice to bury those found *felo de se* in a public cross-road, with a stake driven through the body. This barbarous ceremony was last performed in that year on the body of one Griffiths, who was buried at the junction of Eton Street, Grosvenor Place, and King's Road. The driving of a stake through it was, however, on this occasion dispensed with.

By an Act passed in 1823 the interment in a churchyard or other burial ground of persons who had committed *felo de se* was authorized, but performance of the rights of Christian burial was still prohibited. Under an Act of 1882 any form of orderly religious service may

now be used at the interment of a person who has committed *felo de se*, except that of the Church of England by a minister of the Church of England, since this is forbidden by the rubric. The practice of forfeiting the goods and chattels of a suicide to the Crown originated in Anglo-Saxon times, and was not abolished by law until 1870, though it had fallen into desuetude long before that date. Pepys gives an interesting account of the precautions relatives were led to take in consequence of this cruel practice. Antony Joyce, his cousin's husband, threw himself into a pond at Islington, and, though rescued, was dangerously ill. Pepys went to see the wife, and found her, to quote his words, "in fear that the goods and estate would be seized on, though he lived all this while, because of his endeavouring to drown himself. My cozen did endeavour to remove what she could of plate out of the house, and desired me to take away my flagons, which I was glad of, and did take them away with me in great fear all the way of being seized; though there was no reason for it, he not being dead, but yet so fearful was I." Antony died, and an inquest was opened. After several adjournments, during which Pepys saw the King and endeavoured to get his help, the jury eventually found that the deceased died of a "feaver."

The last point which remains to be considered is the effect of suicide on claims under insurance policies. If a person who has insured his life kills himself, and is not found insane and irresponsible for his actions, the policy is vitiated. Some companies include in their policies a condition vitiating the policy if the insured takes his own life. If there is no such condition the rule of common law is that whether the amount of the policy can be recovered depends on the question whether or not the person was at the time responsible for his own acts. Some companies protect themselves by a clause which excludes the risk of suicide for a certain period of years or months. But most companies pay in the case of death from suicide except where there is reason to believe that the deceased had insured his life with fraudulent intention.

THE MAUDSLEY HOSPITAL.

THE building of the Maudsley Hospital established by the London County Council at the suggestion of the late Dr. Henry Maudsley, who made the munificent gift of £30,000 towards its cost, had just been finished at the outbreak of war. It was lent in the first instance to the military authorities, and later to the Ministry of Pensions for the treatment of neurological cases. Its reorganization for its original purposes is now approaching completion. The hospital is intended for the treatment—entirely on a voluntary basis—of nervous disorders, both organic and functional, and of early and recoverable types of the psychoses. It is designed also for the investigation of cases presenting unusual scientific interest or difficulties of diagnosis, for research into the causation of nervous and mental disorders, and for education. It will, we believe, be the first institution in this country on the lines of the neurological and psychiatric clinics of other countries. The medical staff so far appointed includes Dr. E. Mapother, medical superintendent; Dr. A. A. W. Petrie, deputy medical superintendent; and Dr. W. S. Dawson, senior medical officer. Additional medical officers will be added as the work of the hospital increases, and there will be vacancies for qualified medical men and women as voluntary clinical assistants. Those desirous of acting in the latter capacity are invited to communicate with the medical superintendent. The staff will very shortly be supplemented by the appointment of a consultant surgeon, a gynaecologist, a dentist, and specialists in diseases of the eye, ear, nose, and throat. The association with the hospital of the pathological department under the direction of Sir Frederick Mott assures the application of the most modern laboratory methods of diagnosis and treatment. The hospital will afford facilities for all remedial measures, including physical methods, as well as various forms of psychotherapy. The out-patient department is to be opened on December 4th, in advance of the wards, and cases will be seen there on four days a week from 2 p.m. (men, Mondays and Thursdays; women and children, Tuesdays and Fridays). A charge will be made for attendance as at the general hospitals. Cases with all types of nervous and mental disorder will be eligible as out-patients, but especially those whose symptoms and desire for treatment would render possible their later admission to the wards, if necessary.

SIGHT-TESTING OPTICIANS.

DURING recent months much activity has been observable amongst the sight-testing opticians. There is a strong move on the part of some of them to secure a State register, ostensibly for the protection of the public against the dangers of the more ignorant of their fraternity. The more established of the sight-testing opticians have for some years banded themselves together, through the Spectacle-makers' Company and the British Optical Association, for the conferment of such cryptic appendages as F.S.M.C.London and F.B.O.A. These elder self-examiners view with apprehension not unmixed with indignation the action of another and newer association of opticians which grants "diplomas" after an examination the standard of which they hold in some scorn. This stimulus from within arouses the elder opticians to try to secure their position before they are swamped by the smaller fry. There is also perhaps a stimulus from without. The establishment of a midwives' register some years ago, the more recent formation of a register of nurses, the extension of the dental register, possibly also the registration of teachers, have all stimulated the desire for the protection and status which such a registration gives. The movement has not been overlooked by those best able to judge. We print on page 1084 the report of the Council of British Ophthalmologists on this matter. It is a detailed and reasoned statement; it is simply written and can be understood by everyone. It leaves no room for misapprehension of its purport. The ophthalmic surgeons of distinction and experience who form that Council are of opinion "that any State recognition of sight-testing by persons possessing only an optical qualification would not be in the interests of the community." But it may be argued that this Council by reason of its personnel is prejudiced; being themselves ophthalmic surgeons they may fear that a register of sight-testing opticians would endanger their own calling. Such a suggestion can scarcely be maintained of members of a profession whose interest in the public weal is unquestionable. But there is another basis for judgement. Last week we gave the concluding instalment of a summary of the Report of the Committee on the Causes and Prevention of Blindness. That committee, we understand, dealt with this subject at the request of some of the protagonists of the sight-testing opticians. The committee had a mixed personnel; seven were laymen experienced in public affairs and health matters, four were Government officials, and only three were practising ophthalmic surgeons. This committee, with its preponderance of laymen, without hesitation reported that the proposal for registration of sight-testing opticians is a danger. "The public would regard the register as an official guarantee that those whose names were included in it were competent not only to provide but to prescribe glasses, and generally to deal with defects of vision from whatever cause arising." The organized bodies of opticians who state "that many people who test sight and prescribe spectacles are untrained and incompetent" tell the truth; but the truth is wider than they admit. Their statement is true not only of the chemists, drapers, toy vendors, and petty hucksters who sell glasses to those who will buy: it applies also to their own practice; they themselves are incompetent in the absence of medical training, and sometimes they are the more dangerous by

reason of the "qualifications" with which they seek to reassure the public. Admittedly there is a problem: the provision of a sufficient number of practitioners competent to do eye work. But the cure is not to be found by an increase of sight-testing opticians, but by an increase of medical practitioners trained in the work of refraction. This provision is being brought into being rapidly. The institution of treatment for elementary school children has given it a great impetus. Public authorities can stimulate the provision and make it widely available by arranging that those practitioners who do ophthalmic work for them shall be part-time officers and not whole-time officers, so that in their unofficial time their skill and experience may be at the service of the community generally. Sight is the master sense of man; it plays an ever-increasing part as civilization becomes more complex. No member of the body is more closely knit with the welfare of the body generally, and none is more delicate, than the eye. "Safety first" applies with peculiar force to vision, and that can only be secured by those who would practise eye work undergoing the strenuous discipline in observation and treatment which a full medical curriculum and hospital course provides. There is a subcommittee of the British Medical Association which has this matter under consideration; through it any necessary action for the enlightenment of both public and legislators could be initiated.

THE ART OF VACCINATION.

A POSSIBLE disadvantage incidental to extensive resort to vaccination during small-pox prevalence may consist in the heavy pressure on the time of a busy public vaccinator or private practitioner. If people would only take the trouble to get vaccinated or revaccinated in quiet times there would be no chance of omission of any of the precautions which may with advantage be observed in the operation—the cleaning of the surface of the skin, the use of sterilized instruments, including a blower instead of the operator's lips, and the protection of the vaccinated surface against extraneous infection in vaccinating and in inspecting the result—all as specified in the "Instructions to Vaccinators under Contract" of the Ministry of Health. The private practitioner has the additional responsibility of providing himself with suitable lymph, which duty in the case of the public vaccinator is performed by the Ministry of Health. As regards the art of vaccination, we have asked a public vaccinator of high standing and great experience to give our readers the benefit of his views. They are to the following effect: Primary vaccination has been so standardized by the use of the Government's vaccine and the simple methods of asepsis employed, and accidents are so rare, that occasion does not exist for much further improvement. If a vesicle be accidentally broken or a crust prematurely detached an opportunity for introduction of infection may occur, but that possibility attaches to every scratch of a pin. In revaccination the real difficulty lies much less in the technique of the operation than in the fact that people beyond infancy are not under the watchful eye of the mother, and the site of vaccination is open to all kinds of mechanical interferences which lead to the breaking of the vesicles and possible staphylococcal or streptococcal infection of the vaccinal site. The irregular vesiculations of revaccination are more vulnerable than the full, hard vesicles of primary vaccination, and ought therefore to be protected with special care. Probably not many "bad arms" are due to infection from the skin directly, but to violence of some kind or other; when once the vesicle is open and lymph exudes, germs may get in. The character of the dressing is of consequence in determining whether a vesicle shall break or not. A pad of boric wool over the site, fixed by two strips of rubber plaster or zinc oxide plaster, works well, but sometimes there is a slight adherence to the vesicle or crust when the dressing is removed on the eighth day, or the pad may be damp with lymph. On removing the pad it is a very useful precaution to paint with tinctura iodi mitis, though it may cause smarting for half a minute after application. The iodine hastens the drying of the scab and reduces risk of infection. "Bad arms," however, are often not septic at all, but due to intense reaction tending to choke temporarily the axillary glands, resulting in some degree of lymphatic stasis. In such cases the vesicles are not broken, but become crusts quite regularly. If there is axillary pain, a hot sponge in the armpit gives relief; and if occasionally the skin of the arm is tight and shiny, a hot lead and opium lotion will usually clear up matters in twenty-four hours. If some accident to the crusts should lead to their separation, any small raw surface left may, if dry at the base, be painted with iodine, but if inclined to "weep," a simple antiseptic ointment, or, still better, a moist, warm fomentation may be applied. For preparation of the skin before vaccinating, methylated spirit is suitable and convenient, but iodine washed off with alkaline spirit soap might be worth a trial.

THE STAGES OF HUMAN LIFE.

THE progress of human life from the cradle to the grave is so naturally interesting to all humanity as to have engaged the thoughts and the pens of writers in every age. Few students can have steeped themselves more thoroughly in the literature of the subject than Dr. J. Lionel Tayler; he has fullness of knowledge and a fitness in selection and quotation. The subject has many aspects, and the best known classification of the ages of man is that which Shakespeare put into the mouth of the melancholy Jaques. It is too hackneyed to quote, and we may turn to a new classification which Dr. Tayler has made from a biological point of view. He has written a series of essays marked by knowledge and wisdom and full of judicious advice, and has collected them in a volume[1] published some time ago. For one or two of the stages into which he divides human life he has had to devise new names, which, however, are self-explanatory; they are ante-natency, natency, infancy, weanlinghood, childhood, pubescence, adolescence, youth and maidenhood, maturity, and old age—not seven ages but ten. To whatever period of life a reader has attained he will find much that will be of value in aiding him to govern himself and to regulate wisely his relations with others. In the parts concerned with the life periods through which he has already passed he will probably feel some regret that he had not the benefit of Dr. Tayler's suggestions and guidance—say in the training of his own children and in his attitude to them after they had passed the age for direct parental control, so that they should develop from dependency into companionship. He deals with every stage of life, whether past or current or still to come, in an interesting manner, and the family doctor, who is often the confidential consultant outside the directly medical sphere, will find the volume one to keep on his bookshelf, to be taken down at any time for a quiet hour's browsing. The following exordium addressed to the adolescent, concerning spiritual travellers, may be quoted as a sample of the author's quality, and of how he utilizes his wide reading to help him in his own message: "Or perhaps your sympathies are with another kind of traveller, the enthusiast, the prophet, the seer, and you like the lonely untrodden path not of 'the has been' but of 'the will be.' If so take Lessing with you as your guide and accept one of his warnings. Do not be one of those enthusiasts who egotistically wishes the world accelerated through him; you will be made use of, have no fear of that if you do your part, but remember that that which takes thousands of years to mature will not specially hurry its ways because some human being wants it to come in the moment and only the moment of his existence. You must take disinterested joy in all your journey, and remember to learn, as Herbert Spencer bids us, that in a world so vast as ours, single efforts seem comparatively so very small when we look at them after a few years of striving, or even at the end of our lives, but that little must be felt worth while to us."

[1] *The Stages of Human Life.* London: John Murray. (Demy 8vo. pp. 292. 18s. net.)

THE ROYAL DENTAL HOSPITAL.

THE annual dinner of past and present students of the Royal Dental Hospital of London was held at the Trocadero Restaurant on November 25th, with Mr. P. L. Webster in the chair. After the loyal toasts had been honoured, the chairman presented the scholarships, prizes, and certificates to the successful students. In proposing the toast of the "Past and Present Students of the Royal Dental Hospital and Dental School," Mr. Webster said that during the afternoon he had had an opportunity of visiting the hospital and inspecting the new departments made necessary by the introduction of new branches in dental science and changes of ideas and methods, and he was almost overwhelmed. While agreeing that students should have the highest standard of teaching, he warned them of the danger of specializing too much and losing sight of general principles and also the sense of proportion. He urged past students to make a point of attending the "At Home" held in the afternoon of the day of the annual dinner and to see something of the progress which had taken place during the year, and thus keep in touch with new methods and ideas. One of the great advantages of the annual dinner was that it afforded past students an opportunity of renewing old friendships. The toast was acknowledged by Mr. F. Breese for the old students and by Miss F. H. Bachrach for the present students. The dean of the school, who also replied to the toast, reported the progress made by the school, and certain changes which had taken place. He said that during the year sixty students had obtained diplomas, and that the University of London had decided to continue the school as a school of the University for a further period of three years. The University had also instituted a degree of Bachelor of Dental Surgery. The athletic side of the school had been very successful, and he appealed for subscriptions for the purchase of a recreation ground for the students. The toast of "The Visitors," proposed by Mr. J. G. Turner, was acknowledged by Sir Humphry Rolleston, President of the Royal College of Physicians of London, and Sir Anthony Bowlby, President of the Royal College of Surgeons of England. Sir Frank Colyer proposed the health of the chairman, which Mr. Webster acknowledged. The music and recitations during the evening were provided by students of the hospital.

THE GENERAL MEDICAL COUNCIL.

SIR DONALD MACALISTER opened the winter session of the General Medical Council with an address as lucid as ever, but shorter than usual because the Council has less than its customary amount of work to do. The reason is that it has said its say for the present about medical education and the curriculum, and the matter is now transferred to the licensing bodies, some of which have already taken steps which show readiness to accept the Council's recommendations. The President expressed his confidence that all will come into line, recognizing that the Council's schemes should each be considered by them as a connected and co-ordinated whole, though opinions may differ as to minor details. To one such detail the President made specific reference—to that of what he called "the pre-registration test" in chemistry and physics. He made it plain that the Council intended the test to be in addition to any examination in these subjects at matriculation. A student intending to enter medicine is to complete his school course of general education to the same level as his fellows intending the faculties of arts or pure science, and then to acquire in addition, in his post-school but pre-registration stage, such further knowledge of chemistry and physics as will enable him, immediately after registration, to take up the study of these sciences in their application to medicine. This is a change—we venture to say a reform—of greater importance than may at first sight appear, for it ought to ensure that the schoolboy, whether on the classical or modern side, shall not specialize on quasi-professional subjects, and that he shall, after he has finished his school days and matriculated, go on with the study of these sciences, which underlie the special professional subjects to which the rest of his life is to be devoted. If the purpose is to be justified it must have the loyal co operation of the teachers of these subjects to medical students. The President's observations to these schemes of the Council lent point to his graceful reference to the admirable work done in their preparation by Dr. J. C. McVail before his second term of office expired this year. The revised curricula, Sir Donald MacAlister said, include much that is due to the initiative and perseverance of Dr. McVail, who in this and other ways has left the profession his debtor. The debt has been recognized by the British Medical Association and by the Royal Society of Medicine, as well as by his own university, but it may not be out of place to recall that Dr. McVail was a great public servant the State should delight to honour. The full text of the President's address is published in the SUPPLEMENT this week. It will be seen that the Council welcomed two new members—Sir Humphry Rolleston, representative of the Royal College of Physicians of London in succession to Sir Norman Moore, who has resigned office after twenty-one years' service, and Dr. R. B. Wild, who succeeds as representative of the University of Manchester Professor Roy Dean, recently appointed to the Chair of Pathology, Cambridge. Sir W. Leslie Mackenzie, the new Crown nominee for Scotland, was absent, owing, unfortunately, to illness.

THORACOSCOPY IN SURGERY OF THE CHEST.

THE occasional lecture, which Dr. H. C. Jacobaeus, professor of medicine at the University of Stockholm, gave to the Royal Society of Medicine on November 22nd, when the president, Sir William Hale-White, was in the chair, followed the same lines as that which he gave at Manchester on November 17th, already reported at some length in our columns (JOURNAL, November 25th, p. 1043). During his visit to London Professor Jacobaeus gave two practical demonstrations of his method of dealing with pleural adhesions—one at Guy's Hospital and the other at the Brompton Chest Hospital. In his lecture at the Royal Society of Medicine he dwelt on the practical importance of the thoracoscope, especially in the pneumothorax treatment of pulmonary tuberculosis, and illustrated his remarks by a large number of lantern slides of skiagrams, which showed the excellent results of his method for the cauterization of pleural adhesions under thoracoscopic control. Mr. Geoffrey Marshall, who described a case in which that morning, at Guy's Hospital, Professor Jacobaeus had cauterized pleural adhesions, said that it was particularly noticeable how comfortable the patient was throughout the course of the operation, which was performed under a local anaesthetic. Dr. Vere Pearson congratulated Dr. Jacobaeus on his results, and asked for information regarding the improvement in the clinical condition of the patients after pleural adhesions had been cauterized, as compared with other patients who had not undergone such treatment. Professor Jacobaeus, in reply, recalled his statement that in about 75 per cent. of the cases reported the method was technically successful in removing adhesions which had prevented the complete collapse of the lung; the clinical results were not so favourable, but about 63 per cent. of the patients had been freed from symptoms.

INTERNATIONAL ADVISORY COMMITTEE ON ANTHRAX.

THE Government of the Commonwealth of Australia has appointed Sir Thomas Oliver, M.D., of Newcastle-upon-Tyne, to be the Australian representative on the Advisory Committee on Anthrax of the International Labour Organization of the League of Nations. The other members are: Dr. Gilbert (Belgium), M. Boulin (France), Dr. Frey (Germany), Lieut.-Colonel Hutchinson (India), Professor Loriga (Italy), Dr. Hoshiai (Japan), Mr. R. W. Dixon (South Africa), Professor Roca (Spain), Mr. Ribbing (Sweden). The Government of the United States will be represented in an unofficial and consultative capacity by Dr. M. Dorset of the United States Department of Agriculture. The Committee will meet in London on Tuesday next, December 5th, under the chairmanship of Sir William Middlebrook, the nominee of the British Government. The Committee is instructed to inquire

into the disinfection of wool and hairs infected with anthrax spores, and also into the practice and effective methods of preventing infection among flocks. It is to report on these subjects to the governing body of the International Labour Office in time for the consideration of the International Labour Conference in 1923. It is also to inquire into the possibilities of dealing with infection by anthrax from hides, skins, and other materials. The Committee is prepared to receive representations on these matters, which should in the first place be addressed in writing to Sir William Middlebrook, care of the International Labour Office, 26, Buckingham Gate, London, S.W.1.

INSTRUCTIVE MISTAKES.

IT is admitted on all hands that it is a good thing to learn from our mistakes, and the meeting of the Surgical Section of the Royal Society of Medicine which will take place on Wednesday next, December 6th, at 5.30 p.m., will be given up to hearing from the President of the Section, members of its Council, and several other well-known surgeons, the story of a mistake in diagnosis or treatment. Each instance is to be related quite briefly, each must have befallen the surgeon himself, and the lesson to be learnt from it is to be pointed out. The details of these cases will not afterwards be published. It ought to be a most interesting meeting and we foresee a large attendance. Surgeons wishing to take part in the meeting by relating instructive mistakes of their own are requested to communicate with the Junior Secretary, Mr. Philip Turner, addressing him at the Royal Society of Medicine, 1, Wimpole Street, London, W.1. A good many years ago Mr. Ernest Hart, then Editor of this JOURNAL, established a column which he called "The Confessional," for the receipt of reports of mistakes. This column started fairly well, but it very soon became apparent that most of the contributors to it wished to relate the mistakes of other people, and after a short trial it had, on this account, to be given up. We wish the President of the Section, Mr. James Berry, success in the rather difficult task he has set himself of presiding at a "mistakes meeting."

SIR CLIFFORD ALLBUTT has recently accepted the position of President of the West London Hospital Post-Graduate College. In accepting the invitation and wishing success to the College, Professor Clifford Allbutt, whose interest in post-graduate education is well known and whose recent lectures at the College on "Kinds of pneumonia" and "Angina pectoris" attracted large and appreciative audiences, expresses his conviction that the future of medicine in Great Britain depends upon the continued development of general practice and its opportunities.

Medical Notes in Parliament.

[FROM OUR PARLIAMENTARY CORRESPONDENT.]

Conditions in the Near East.—In the course of the debate in the House of Lords on November 23rd, on the address in reply to the King's speech, the Archbishop of Canterbury referred to conditions in the Near East. He was in closest touch with the Patriarch of the Orthodox community. There were at this moment a million and a half persons the great proportion of whom were not members of the poorer classes a little while ago, but were to-day literally without the means of subsistence or shelter or a home of any kind. The matter called for the thought of European statesmanship and the intervention of European funds if appalling dangers were to be stayed—dangers of pestilence which might spread to a degree that it was impossible to calculate. He was receiving constant accounts from the Piraeus and Athens, where the floors of the ordinary goods sheds and stations were covered with people sitting down on them without food or adequate covering. The conditions at the ports were almost beyond belief. He read a telegram giving an account of 50,000 persons who had been travelling on foot for ten days, the majority without food. The rain and cold increased the suffering and were causing many deaths. An utter lack of sanitation threatened cholera and typhoid. Scarlet fever had broken out. The services of doctors, nurses, and medicine were imperatively needed. The greatest suffering was occurring among the babies owing to lack of milk.

The Medical Group.—The four surviving members of the medical group in the last House of Commons have invited the nine newly elected medical members to dinner in the House next Monday, and from this gathering, doubtless, the group will again be constituted.

NOTES ON SMALL-POX.

BY

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GENERAL OUTLOOK.

To keep himself posted in a general way about the current position of small-pox is an essential for every medical practitioner. A table giving the deaths from small-pox in England and Wales (London deaths recorded separately), and the admissions to the hospitals of the Metropolitan Asylums Board, from 1881 to 1921, together with the total cases certified for the years 1911–21, was printed in the JOURNAL of November 11th at page 943. The following figures give the number of cases recorded this year down to November 28th: Cases certified in England and Wales, 890 (approximately); total deaths, not yet ascertained; London deaths, 20; admissions to Metropolitan Asylums Board hospitals, 62.

All the 1922 London cases have occurred since the end of July; that is to say, for the first six months of the year London was clear of small-pox. How it was introduced is unknown. The first known case fell ill on July 1st and was overlooked until August 3rd, when he was discovered owing to the occurrence of a group of secondary cases; it is probable that infection came from the Continent, and possibly by means of a London resident returning infected from a visit there.

It will be noted that the death rate is over 30 per cent. London proper and parts of the home counties are inseparable so far as small-pox is concerned, for it occurs in them without respect of boundaries; the figures for the wider area are therefore of importance; they show 75 cases and 24 deaths for 1922. The rest of England, mainly the North, has had nearly 1,000 cases which have been proceeding steadily throughout the year. These have been of a light type, only one death having been reported in 700 cases. This latter type is often spoken of as "aberrant" or "atypical," phraseology not justified by the facts. Severe and mild epidemics of small-pox are equally classical, being recorded by Sydenham, van Swieten, Jenner, and many others; the mild epidemics have comprised cases which certainly must be reckoned in millions; the type is of equal interest in diagnosis, inasmuch as it displays the distribution which is characteristic of the disease.

Guiding Points in Small-pox Diagnosis, with Illustrative Cases.

If I were discussing the subject with junior assistants whom I wished to arm with sound equipment, I should beg each one of them first of all to do three simple things, which, in fact, I should make obligatory: (1) bring his own state of vaccination to date; (2) understand the few simple facts about the repeated invasion of small-pox into the country; (3) know exactly where he can get further information about small-pox. As a rule these last two points are ascertainable from the respective medical officer of health.

I should then counsel him most emphatically to place this question in his mental armoury for use during the rest of his life: "Can this case before me possibly be small-pox?" That is, he should use that test question, amongst others, in respect of every single case the diagnosis of which has not been positively made. I should tell him that while he might put this question one thousand times and have "No" for an answer, the one thousand and first case might be small-pox. That probably he would never see a case of small-pox in his life, but that the present position is such—it being now not to the point whether it be reasonable or not—but in fact is such that a single "missed" case may result in hundreds of deaths, and in hundreds of thousands of pounds sterling being spent; that in consequence of the mass of the community having divested themselves of their individual anti-small-pox protection—namely, their immunity obtainable from vaccination—an almost inconceivable strain is thrown upon our profession which is more than any human flesh and blood should be asked to undertake; that is the obligation for every one of us instantly to recognize every single case of small-pox which may be presented to him, a watch requiring an almost inconceivable degree of perfection, so that we are to be right one hundred times in one hundred. That is the task which is set us under pain of letting in a devastating and diabolical invader, an effort which we could hardly undertake to continue were it not that the laity, at last

perceiving the extreme gravity of the situation, is slowly coming to our assistance in the matter by means of the individual protection afforded by vaccination. So much it is necessary for us all to realize.

This, then, is our first and invariable item of equipment, "Can this be small-pox?"

I should then try to place my friend in possession of the questions with which I try to follow this up. Assuming that the case is small-pox and must be proved to be such, can a definite short illness be shown, not necessarily acute in the sense of being fulminating or even severe, but a definite short illness followed after about three days by definite blemish of the skin? Can this be shown? Can papules be shown, or less commonly an erythema, or a purpura? Can a relatively severe degree of initial prostration be shown? Does the rash, however scanty or dense, possess nevertheless a characteristic distribution? A characteristic depth in the skin? A characteristic maturation?

Those are some of the questions to be answered. I should further remind my audience that their position, happily for them, seldom requires an exact and final diagnosis, and they may be pleased to refrain from racking their equanimity to that extent; that what is usually required is a prima facie case with the clear grounds of their suspicion, which will warrant an appeal to their respective medical officer of health.

My readers may perhaps permit me to recite the features of two cases, both small-pox, which were recently presented to me.

The first was that of a young married woman, aged 28, who had eaten some unusual fish, part of a skate, on a Saturday and on the Sunday and Monday had had vomiting and a good deal of aching and pain in the back; a definite but not very profuse rash on the Tuesday, which was far from inconsistent with a papular urticaria. The elements were soft and hardly palpable, and there were some few irregular patches of erythema. I saw the case for the first time on the Wednesday, when the rash was stated to present much the same appearance as on the day before except that there was now more of it; the whole picture obviously and strongly suggested small-pox, but rather resembled the rare acute general papular erythema which is one of the cleverest mimics of small-pox there is. On this second day of the rash, assuming the case to be one of small-pox, there was a most remarkable delay in its maturation, there being no obvious commencing vesiculation.

The next day there was still, in the difficult half-light and natural hindrance to complete examination in a cramped room, no obvious vesiculation, an uncommon feature in my experience in an attack of small-pox of this degree of severity, as judged by the papules, which were numerous but discrete. At the same time more spots had appeared, both on the face and hands; the circumoral skin, for instance, which at first had been remarkably clear, though the skin in that region was irritated, was now showing papules. Evidently some spots had come out on the face and upper extremities on the Tuesday, others on the Wednesday, and others on the Thursday; on this Thursday, the third day of the rash, the spots were soft and insignificant papules, compatible certainly with the first day of a small-pox rash, but very uncommon for a third day; there was, however, one lesion over the sacral region which had excited suspicion from having somewhat the appearance of vesiculation, though it was hardly palpable. There were some erosions on the soft palate which, by the Thursday, had coalesced and presented a condition almost of ulceration. Generally speaking, the rash strongly resembled that of variola at the end of the first twenty-four hours, which had then come to a full stop.

Nevertheless, the case for small-pox could be sustained (*a*) by the relative distribution of the rash, which was characteristic, by its abundance on the face and forearms, and by its scantiness on the chest; (*b*) by the severe initial prostration; and (*c*) by very faint and yet unmistakable early signs of vesiculation among the lesions on one of the forearms. Accordingly she was certified, and so resulted.

So much delay in the maturation of the rash is uncommon; the rash itself could neither be called shotty, though it had a degree of firmness, nor had it that velvety quality occasionally seen in some ill-developed small-pox rashes and very severe attacks; this attack, as indicated by the number of spots, did not portend at first at least extreme severity.

The case illustrated once more three very well ascertained factors in diagnosis: the comparative unreliability of a "history," the reliable nature of early prostration, and also of the distribution of the rash. In my experience such anomalies of the rash as this case presented often depend on the individual constitution of the patient or the skin; I was not surprised, therefore, to hear the patient, who did not look robust, say in answer to a question that she had previously had an attack of enteric fever. She had never been vaccinated.

The second of the two cases mentioned, also small-pox, presented not the slightest impediment to diagnosis. She had been intimately exposed to infection on the 8th of the month, and had been vaccinated on the 13th. Most fortunately for her, the vaccinia had apparently run a rather more rapid course than usual, and the rash of small-pox which she developed on the 22nd of the month was discrete and benign in every way, being much modified by her vaccination. Nevertheless, the distribution of the twenty or twenty-five spots which she had was entirely characteristic and unmistakable, as was also the full vesico-pustular appearance of some of the pocks.

These two cases are an illustration of what I meant by saying (BRITISH MEDICAL JOURNAL, November 25th, p. 1045) that the vaccinal condition serves rather to facilitate than to obscure diagnosis, and that the most puzzling cases are more apt to derive their obscurity from some idiosyncrasy of the individual patient.

England and Wales.

A MEDICAL ART PATRON.

THE history of the royal borough of Reading, and particularly of its ancient abbey, owes much to the researches and archaeological enthusiasm of Dr. Jamieson B. Hurry. He has again put Reading in his debt by presenting to the town a picture, painted by Mr. Stephen Reid and exhibited at the last Royal Academy, representing the appointment of the Mayor of Reading, from among three burgesses nominated by the Guild Merchant, by the abbot of Reading Abbey, John Thorne, in 1460. As will be remembered by those who saw it at the Academy exhibition, the painting is a vivid reconstruction of an interesting historical episode. Reading was a town that had grown up around an abbey, and only after a bitter struggle for two hundred and fifty years did the burgesses, being under the authority of the abbot, acquire the privilege of self-government which other English boroughs were enjoying. Eventually peace was restored by King Henry III, who granted a charter of incorporation to the Guild Merchant, and an agreement was drawn up by which the burgesses acknowledged the abbot's right to appoint one of three burgesses selected by themselves to be the *Custos Gilde* or mayor, who should take an oath of fidelity to the burgesses as well as to the abbot. The scene of the painting is laid in the abbot's memorial hall, at the inner gateway of the abbey, which is still standing.

SMALL-POX IN LONDON.

Constant search for and vaccination of contacts, surveillance of them until the small-pox incubation period had passed, together with immediate hospital isolation of discovered cases, and free resort to vaccination on the part of an appreciable section of the general public, have had the effect of checking the threatened epidemic of small-pox, and of giving grounds for the hope that success in arresting the threatened outbreak of the disease may be achieved. It is particularly satisfactory that Poplar, the borough in which vaccination has been more neglected than anywhere else in London, and in whose workhouse the outbreak has taken place, should now be awake to its danger, and have taken much advantage of the offer of protection. But the danger is not at an end. It has been a frequent experience that epidemic small-pox has been slow in developing, that months have elapsed during which sporadic cases have occurred before the bursting of the storm. That was the London experience of 1901. As recorded in Dr. J. C. McVail's Milroy lectures in 1919, the following were the monthly admissions of cases to hospital—at the beginning of the year there was already one case:

January	2	July	14
February	1	August	82
March	0	September	167
April	0	October	272
May	1	November	438
June	5	December	761

In the great epidemic which unvaccinated Gloucester went through in 1895–96 the following was the course of events:

Month.	Cases.	Month.	Cases.
1st	1	9th	145
2nd	0	10th	604
3rd	3	11th	733
4th	1	12th	283
5th	3	13th	122
6th	7	14th	13
7th	12		
8th	52	Total	1,979

In Gloucester the pestilence was not stopped until it had become the best vaccinated city in England.

Dr. Seaton, in his book on vaccination published in 1868, pointed out that the stories of Cardiff and Sheffield in 1857

were similar. He regarded it as characteristic of all small-pox epidemics, but there, as after events proved, he was mistaken; the Edinburgh epidemic of 1903–4 showed no such hesitation in its onset. The lesson, however, is that throughout the winter which has now begun the public authorities concerned—namely, the Guardians and the Borough Councils—should in no degree relax the efforts in which they have so actively engaged to protect the populations for which they are responsible.

It is good to learn that meanwhile the Education Committee of the London County Council is exercising special vigilance over schools in the affected area. In Poplar every absentee in a group of fourteen schools is being followed up by the divisional medical officer and the borough medical officer; the scheme is working smoothly; the head teachers of the schools in question have been given any necessary advice as to vaccination of pupils, and arrangements have been made for the public vaccinator visiting thirteen of them. Under the present law there can be no compulsion to vaccination, but it is right that the offer should everywhere be freely made.

CENTRAL MIDWIVES BOARD.

A special meeting of the Central Midwives Board for England and Wales was held on November 16th, with Sir Francis Champneys in the chair. Eight cases were down for hearing and the Board removed three of the midwives from the Roll. At the ordinary monthly meeting held next day the Standing Committee considered a letter from the Macalpine Maternity Home, Manchester, forwarding a copy of the following resolution:

"The Committee of the above Home desires to urge upon the Central Midwives Board its conviction of the need for a longer and more adequate training for midwives. It asks the Board to give immediate attention to this matter and urges them, before any change is made, to make careful investigations into the methods and scope of training in other countries and into the needs of all classes of institutions employing midwives."

It was agreed to inform the Macalpine Maternity Home that the Board has already under consideration the question of lengthening the period of training. To a letter from the Central Midwives Board for Scotland it was agreed to reply:

That in the opinion of the Board it may be a matter of extreme difficulty for a Local Supervising Authority to inspect satisfactorily in respect of cases, taken in the area of another Local Supervising Authority, as the Local Supervising Authority of the area in which the cases are taken is likely to have the better knowledge of them. The Board thinks, however, that the matter might be satisfactorily adjusted if the Local Supervising Authorities concerned were to come to a working arrangement on the subject as is done, with good results, in many areas in England, as, for instance, the counties of London and Middlesex and in other adjacent areas.

The report on the work of the Board for the year ending March 31st, 1922, was considered and it was decided that after amendments and signature by the Chairman and Secretary it be forwarded to the Ministry of Health.

Scotland.

GLASGOW STUDENTS' HANDBOOK.

THE issue for 1922–23 of the *Students' Handbook*,[1] published at Glasgow University under the auspices of the Students' Representative Council, has appeared. The intention of this volume is mainly to enlighten the students of Glasgow on many matters which, on their entrance upon academic life, it is to their interest to know, and a great deal of information is given in it regarding the innumerable students' societies and clubs. The volume is prefaced by a little story told inimitably by Mr. R. B. Cunninghame Graham, the moral of which is that "a university training gives a man the arms with which to face life, but he has to learn to use them himself." The Student Welfare Scheme of the University is commended in an introduction by the Principal, Sir Donald MacAlister, and articles on the different faculties, and on such subjects as the O.T.C. and the higher Civil Service examinations, are contributed by authorities. In the section devoted to the Faculty of Medicine Professor E. P. Cathcart reminds his readers that the profession of medicine is going to be a crowded career, and that, although undoubtedly it is a magnificent career, the practice of medicine is difficult and its disappointments many; it calls for enthusiasm of a robust type. Medicine, he continues, is not an art to be acquired in the few years of the student curriculum. These are merely years of elementary apprenticeship. The real knowledge, the knowledge which will be of inestimable value, is mainly obtained during the first few years following graduation, provided they are rightly used. It is rare, he says, to find the student who has really grasped and fully appreciated the fact that the curriculum, as at present designed, is not drawn up at random for the gratification of a body of pundits out of touch with reality; the presence of each subject in the course, its position in the course, and the amount of time to be devoted to it, have all received the most earnest consideration. The volume is distinguished by a cover design by Mr. Louis Raemaekers and contains many excellent photographs. It is edited by Mr. H. H. Livingstone, and he and his undergraduate committee are to be congratulated on the result of their efforts.

[1] *Glasgow University Students' Handbook, No. XLII, 1922–23.* Edited by H. H. Livingstone. Glasgow: The Students' Representative Council of the University of Glasgow. 1922. (Cr. 8vo, pp. 152; illustrated.)

ABERDEEN MEDICO-CHIRURGICAL SOCIETY.

The annual business meeting of the Aberdeen Medico-Chirurgical Society was held in the Society's hall on Thursday, November 23rd. The following office-bearers were elected:

President, Dr. Alexander Ogston; Vice-President, Sir H. M. W. Gray; Secretary, Dr. G. M. Duncan; Treasurer, Dr. George Rose; Assistant Secretary, Dr. H. Edgar Smith; Recording Secretary, Dr. H. Ross Souper; Editor of *Transactions*, Mr. G. H. Colt. Members of Council: Dr. J. Scott Riddell, Dr. George Williamson, Dr. Henry Peterkin, Dr. Robert Richards.

GLASGOW SEWAGE DISPOSAL.

At the weekly meeting of the Glasgow Medical Lunch Club, held on November 23rd, the guest of honour was Mr. F. W. Harris, F.I.C., analyst to the city of Glasgow. After lunch he gave an interesting address on the modern methods of sewage disposal. He pointed out that Glasgow had to deal with a dry-weather flow of 90,000,000 gallons, and he described the methods of disposal formerly in use and the improvements therein introduced in recent years. He showed how the most recent methods were really natural methods artificially intensified. The system of activating sludge by the introduction of certain insects into the media was first employed in Glasgow in 1921, and by August of this year five filters showed successful colonization. The effect of these insects saved the corporation thousands of pounds, and their efficiency resulted in a very appreciable reduction in capital expenditure on plant. The process was still in its infancy, but it gave promise of notable success. He also made reference to the high manurial value possessed by the sludge following the use of modern methods, and to its use commercially as a fertilizer. The annual return therefore in the future from this source was likely to prove a very valuable asset to the local authorities.

EDINBURGH SURGICAL APPLIANCE SOCIETY.

Sir Montagu Cotterill presided at the annual meeting of the Surgical Appliance Society in Edinburgh on November 24th. The annual report, submitted by Miss S. Malcolm, honorary superintendent, stated that during the year 237 appliances had been supplied, as against 291 in the previous year. As compared with last year only half the amount of work had been done for ex-service men, but the number of splints supplied to civilians was doubled. The amount received for splints was £153, an increase of about £25, which was accounted for by the appliances being on an average larger and more costly than previously; when the cost of materials was deducted there was only a balance of £78 towards the working expenses, which amounted to £162. Although the whole of the work was done by voluntary workers, the society was unable without outside support to cover working expences. Sir Montagu Cotterill said that complaints had been made by some instrument makers that it was not fair and right that a society of this kind should compete with them. To take a fair view of the matter, he believed that the voluntary workers of the society who chose to spend their time and energy in making splints and other appliances for poor and necessitous people, at a price which suited their pockets, were doing a charitable work at which no one could cavil. If the society were to supply a class of patient able to pay a reasonable fee to an instrument maker then he thought it would go beyond what was right; but so long as members of the society were doing charitable work they were entirely within their rights, and that should be the basis on which they stood. The

society should make it clear to surgeons who sent it orders that it was not prepared to give them these splints at the usual price, or anything approaching it, unless they could assure the society that those patients were in such a financial position that charitable help was appropriate. Mr. Pirie Watson said that the only way he saw out of the difficulty was for the society to be accommodated in a hospital, and to become, as it were, a voluntary staff attached to a hospital, such as the Sick Children's Hospital. The chairman said that it would be worth while seeing whether the Sick Children's Hospital would entertain such a proposal. He quite agreed that it would be a good way of carrying on the society.

Ireland.

Ulster Medical Services.

Dr. John Campbell, M.P., at the meeting of the Ulster Medical Society on November 16th, called attention to the position of the medical services under the Government of Northern Ireland; he desired the support of the Ulster Medical Society to help the medical members of Parliament to remedy the position. (1) The salary of the chief medical officer was £1,000, rising to £1,150; the parliamentary counsel to the Ministry of Finance received £1,200, rising to £1,500. The two medical inspectors received, on a basis, £500—a salary fixed twenty years ago, and they now had to make inspections of all medical services; their duties had much increased, but not their salaries; clerks formerly in receipt of £500 a year now received £1,000. The prospects of promotion for the medical officers were also substantially reduced. (2) The Ministry of Labour had now charge of the administration of the National Insurance Act; formerly there were three medical men employed, now there were none. (3) The office of Registrar-General was always held by a medical man, and this was very suitable, considering the technical work; it was now under the Ministry of Finance, and the duties were discharged by a layman. (4) The very inadequate, unequal, and unfair salaries which were still being paid to medical officers in some of the unions in Northern Ireland should be reconsidered. The various unions should be placed on a more uniform and equitable basis. He moved that a committee should be appointed to draft resolutions on the points under discussion and to submit a proposal for the appointment of a permanent medico-political committee. This resolution was seconded by Dr. Morrison, M.P., and carried unanimously.

Coombe Maternity Hospital, Dublin.

The report presented to the annual meeting of the Coombe Maternity Hospital, Dublin, showed that the ordinary income of the year was £5,707, but by the receipts from the hospitals fête and the National Relief Fund, and bequests, the total was raised to £9,954. The total expenditure amounted to £6,399, but this included the purchase of premises adjoining the hospital for £234. Owing to the special efforts made the deficiency, which last year was £4,907, was reduced to £1,352.

Dr. Louis Cassidy, master of the hospital, in moving the adoption of the report, said that in four years the hospital would celebrate its hundredth year, and any hospital that had been before the public for so long a time needed no further recommendation. He impressed on the meeting the importance of further apparatus for dealing in a scientific way with disease. He appealed especially for funds to provide an *x*-ray installation in the hospital. Five hundred women died every year in Ireland from cancer of the womb; of these, a large proportion could be saved if the hospital had the necessary scientific apparatus and an *x*-ray department. The apparatus would cost £600. A research laboratory also was needed, and that would cost £400 a year. A number of people who used to support the hospital had left the country for one reason or another, and another class of people had arisen who did not seem fully to recognize the responsibility they were under to support it.

The chairman said that the Coombe Hospital deserved the most earnest support of all classes and denominations. The institution was pre-eminently a city hospital, and it had been provided in the Charter that the chairman and vice-chairman should be the Lord Mayor and High Sheriff respectively. The report showed that the number of cases treated during the year was practically 7,000. That fact alone should make the citizens rally to the support of the hospital. He suggested that they should make every effort to establish a pre-maternity department and an infant welfare department. The Edinburgh Maternity Hospital had such departments, and they had proved a blessing to mothers and infants. Workers should also be asked to pay twopence a week of their wages towards the support of hospitals, to which the employers should also give a contribution. He also appealed to the merchant princes to lend their aid to the governing body to provide the scientific equipment needed. Sir John Moore, who seconded the resolution, agreed with the chairman as to the necessity for an organization to provide for mothers before pregnancy and for infants newly born. Infant mortality was higher in Dublin than it should be; this was due to ignorance, though not wilful, on the part of mothers as to the care of infants. The main support of hospitals should come from the people voluntarily, but he agreed that appliances should be provided by the State. The *x*-ray installation in the Meath Hospital cost £600, but that was not a fair charge on the funds of any hospital. Sir John Moore concluded by paying a tribute to the excellent staff in the Coombe Hospital, and to the good work done by them.

Correspondence.

PREVENTION OF PUERPERAL INFECTION.

Sir,—Nearly every year a valuable paper by an expert appears in the Journal lamenting the frequency of puerperal infection. May I as a general practitioner draw attention to three points which in practice are very often neglected?

The first is the thorough washing out of the rectum by an enema or enemata in the early stage of labour. That it often encourages a hesitating os to dilate freely, that it gives more room in a forceps operation, and that it cleanses a part into which the "field of operation" occasionally extends is well known to everyone. Why is it then not a matter of routine in all confinements? Why is it not made obligatory on all midwives and nurses in the preparation of a case?

The second point is the proper use of soap. Ordinary soap is not a disinfectant, nor even a detergent *per se*. It merely disturbs the cohesion between dirt and the skin. To illustrate. I have seen a practitioner dip a piece of soap in water and rub it vigorously over the nates and vulva. Thereupon he made his examination, having used the only available hot water to wash his hands. Again, some years ago a writer in a medical journal remarked that he was so impressed with the value of soap as a cleansing agent that he was always careful in making a vaginal examination, having washed his hands, to take up a quantity of soapsuds on his finger before introducing it. Soap without running water or many changes of water is often a delusion and sometimes a snare.

The third point is the avoiding of contamination of the hands in general practice. For pus some sort of protective swab is always available, and for the examination of a body cavity a rubber finger stall is essential.—I am, etc.,

Westcliff-on-Sea, Nov. 20th. J. C. Smellie.

Sir,—Dr. Maclean has rendered a very important service by his presidential address to the Cardiff Medical Society (British Medical Journal, November 18th, p. 976) pointing out the terrible mortality rate of puerperal fever. No doubt more might be done in the way of prophylaxis—for instance, the putting of the infant to the breast at the earliest possible moment, which not only stimulates the production of milk and so benefits the baby, but also produces powerful contractions of the uterus with consequent expulsion of clots, shreds of membrane, and so on. But, in spite of all prophylaxis cases will occur. Many patients have microbes in their circulation which find in the uterus after parturition a place of low resistance. With our present resources there is no need whatever for such a mortality. In the Rotunda Hospital, while Dr. Tweedy was master and Dr. Rowlette pathologist, the death rate from puerperal fever was reduced to a very small percentage. In my own practice during the past twelve years not a single case I have been consulted about has died! Many of these cases were in cottages far distant down the country, and some were in similar dwellings in the city. It is generally thought that the manufacture of an autogenous antigen (vaccine) for such cases is a slow process. It is nothing of the kind. I have often received uterine swabs at 12 o'clock in the morning, and had the doses

of antigen a hundred miles down the country by 3 o'clock the next afternoon. It is of the utmost importance that the material for culture should be taken from the uterus before any douching of any kind has been used.

I feel very strongly about this matter, and assert again, as I have often done before, that no doctor can be considered to have done his duty to his patient in this condition who has not employed this method of treatment, for no other method has given any material results.—I am, etc.,

W. M. CROFTON,

November 24th. University College, Dublin.

THE LIGHT SENSE WITH REFERENCE TO NAVIGATION.

SIR,—A month ago (October 28th, p. 783) an excellent paper was published on the above subject in this JOURNAL; the author, Dr. Freeland Fergus, is a well-known yachtsman, and for that reason his views demand close study. The most noteworthy points that he emphasizes are these:

(1) The inadequacy of our ordinary tests, which determine only macular vision; and

(2) The importance of good field vision, which depends very largely upon the seaman's light sense.

Our present tests for seamen on watch are too severe with respect to macular vision, and will not detect a contraction of the field of view nor any failure of light sense. And yet without good peripheral vision one will not see what to look at. Peripheral vision, though very ill defined, is extraordinarily sensitive to a difference between light and shade, and it is quite independent of any refractive defect. I have found that on a very dark night both I and a myopic (— 8 D.) friend without his glasses could see equally well distant objects; indeed, it will be found that motorists and bicyclists will see far better on a dark night without their glasses than with them. This is no doubt due to the fact that a considerable part of the incident light (17 to 20 per cent.) is reflected and absorbed by the glasses, and in a very dim light the "marginal utility of the commodity," to use an economist's term, is very high.

I note with pleasure that the author states his strong preference for Landolt's broken-ring test types, which I have strongly urged that the Council should recommend as the standard test for macular visual acuity; it is international, and is well adapted for illiterates.

Neurologists should be very grateful to Dr. Fergus for urging them to test the light sense of their patients. A defect of the light difference test is probably the earliest symptom of a lesion in the optic nerve; it will reveal a retrobulbar neuritis, which most physicians neglect, as it is not associated with the obvious signs of a choked disc, and yet pathologically it has the same significance. A retrobulbar neuritis is merely a choked disc which owing to anatomical peculiarities occurs further back, usually at the optic foramen.—I am, etc.,

Newcastle-upon-Tyne, Nov. 27th. ARCH. STANLEY PERCIVAL.

THE TREATMENT OF ACUTE SALPINGITIS.

SIR,—The operation which Mr. Aleck W. Bourne advocates (November 18th, p. 998) is useless for the purpose which he has in view—namely, the prevention of sterility—because the adhesions in the drainage area will almost certainly prevent the ovum from getting into the tube. It is mischievous, because, if the other tube be healthy, pelvic drainage is very likely to cause adhesions which will destroy its function. It is also likely to be a cause of vexation to both surgeon and patient, because the secreting lining of the split tube may cause a sinus in the track of the drain. If we desire to give a patient suffering from suppurative salpingitis the best chance of future pregnancy, we must avoid drainage. The bulk of the tube must be removed; a new mouth must be made for the portion left; and the abdomen must be filled with saline solution and closed without drainage. This procedure attains the three objects mentioned by Mr. Bourne. His own method does not.

As regards the analogy between an inflamed appendix and an inflamed tube, the facts are: In a well-defined case the inflamed organ, whether appendix or tube, forms a bag of infective material. Either may burst and quickly cause death. Either may form a localized abscess, abdominal or pelvic. Either may temporarily recover and become subject to recurrent acute inflammatory attacks. Either may permanently recover and give no further trouble. There is such an obvious similarity between the two organs when inflamed that it is proper to remove them when the attack is severe and dangerous. The surgeon no longer poultices the acutely inflamed appendix. The gynaecologist continues to poultice the equally acutely inflamed tube by means of hot douches and perhaps vaginal tampons. The inconsistency of the gynaecologist is sometimes seen when he opens the abdomen to remove what he has diagnosed as an acutely inflamed appendix and finds the cause of the trouble to be, not the appendix, but an inflamed tube. He then removes the tube. It seems strange that he should remove the tube when he comes upon it by accident, and should so strongly object to operate upon it when he knows it to be the seat of the trouble.

My critics are confused. Possibly their state of mind results from the fact that the appendix seems to have no important function, while the tube is necessary for reproduction. They forget that a tube which is the seat of an acute or chronic pyosalpinx, or even of a hydrosalpinx, has lost its function and has become as useless as an appendix. They also forget that operation on such a tube affords the only hope of restoring its function. Some of my critics may possibly be influenced by the fact that it has become customary to remove the appendix when the evidence against it is very slight, and indeed to execute it frequently on suspicion. They fear that the poor tube may get the same scanty measure of justice. This is no argument against the contention that a badly inflamed tube should be operated on as soon as possible. That the surgeon is an appendix-snatcher is no reason why the gynaecologist should become a tube-snatcher.

When I was honoured by an invitation to open the discussion on this subject in Glasgow I knew that I had no need to go out of my way to be provocative. I had only to follow the trend of much of the most recent literature and of my own thoughts to excite opposition. "My head is bloody, but unbowed."—I am, etc.,

Belfast, Nov. 21st. JOHN CAMPBELL.

THE ALEXANDER-ADAMS OPERATION.

SIR,—In common with a large number of readers I have read with interest the summary of Dr. Bethel Solomons's presidential address at the Obstetrical Section of the Royal Academy of Medicine in Ireland on tuberculosis of the female pelvic organs (BRITISH MEDICAL JOURNAL, November 25th), with the subsequent discussion (taken part in by physicians and surgeons as well as by gynaecologists of renown), which cannot but be of mutual benefit, especially on a subject like this which overlaps all departments.

I have no criticism to make on the general subject of the discussion, which will well repay perusal, but I would take exception to a statement made by Sir William Smyly and endorsed by Dr. Solomons, that he hoped the paper had given a death-blow to the Alexander-Adams operation. I have not of course had the advantage of reading Dr. Solomons's paper in full, but I would protest strongly against such a sweeping condemnation of an operation which has a useful rôle, albeit a limited one, in gynaecology.

The Alexander-Adams operation has fallen into disrepute mainly from the fact that it has been done so often in unsuitable cases—surely no reason for discarding it when performed with judgement and ordinary prudence. I shall not here enter into the indications and contraindications for the operation, but would only say that a careful pelvic examination, if necessary under an anaesthetic, can in practically all cases eliminate the conditions which would render the operation unsuitable or undesirable.

Dr. Solomons states that he has opened the abdomen in several women suffering from tubal disease on whom the Alexander-Adams operation had been performed. That merely shows that the operation had been performed in an unsuitable case, or that tubal mischief had developed later. No one deprecates the indiscriminate resort to the Alexander-Adams operation more than I do, but I would equally deprecate the indiscriminate condemnation of an operation which has proved itself of value in certain cases even in these days when the peritoneal cavity is not always opened with discrimination.

I have occasionally had to open the abdomen after an Alexander-Adams operation where an ovarian cyst or an ectopic pregnancy had subsequently developed, but manifestly the Alexander-Adams operation was not to be blamed for that.

I have invariably found that the Alexander-Adams operation stands the strain of subsequent pregnancy better than

any of the intra-abdominal operations on the round ligaments, and I have seen no instance of failure, even after three subsequent pregnancies. As an indication of the limited number of cases suitable for the Alexander-Adams operation, I would say that in a large yearly operative turn-over in hospital and private, perhaps about twelve cases will be found where the operation can be really recommended. Peradventure even twelve successful cases per annum in the experience of one operator may lead Sir William Smyly and Dr. Bethel Solomons to withhold their threatened death-blow from the Alexander-Adams operation.—I am, etc.,

JAMES HAIG FERGUSON, M.D.,
F.R.C.S.Edin.

Edinburgh, Nov. 26th.

TREATMENT OF FEVER.

SIR,—I have read with interest the letter in your issue of November 18th (p. 1000) containing arguments in favour of treating various acute diseases with a compound powder containing aspirin gr. x, phenacetin gr. v, and pulv. ipecac. co. gr. v.

My experience with this combination of drugs in acute specific diseases and in all conditions of acute toxaemia has been very similar to that described by Surgeon Commander Parnell and others. In my opinion the importance of this line of treatment cannot be overestimated.

As I understand it, recovery from acute toxaemia (any acute disease) is due to that increase of resisting power which we call "acquired immunity," and that the essence of such acquired immunity is an habituation to the particular toxin of the disease from which the patient recovers—just as a man becomes used to nicotine or a horse to diphtheria toxin.

There are three ways in which an individual may become habituated to a toxin: (1) by a huge and continuous dose, as in disease—a dangerous method; (2) by weakening the toxin and so providing stepping stones for reaction, as in vaccination and serum treatment; and (3) by giving small doses of the toxin, as in tobacco and opium smoking and in those cases in which individuals remain immune to a disease (for example, yellow fever) as long as they dwell in a country where it is prevalent but acquire it after return from a country where it is not prevalent.

This new treatment applies the third method. By means of it toxins are continually withdrawn in the sweat, so that the individual experiences a series of small doses. The applications of the treatment are more numerous, and it is more easily applied than the serum treatment. At any rate it opens out a new line of inquiry and ultimately may prove as useful as the serum treatment itself. In conjunction with serum treatment (for example, in diphtheria) it is admirable.

Doubtless there are injurious ways of lowering the temperature, and it is an axiom in medicine that the temperature in acute diseases should not be too much lowered by artificial means; but only those who have employed this treatment when themselves suffering from acute disease are able to appreciate the extraordinary and immediate relief and benefit which follows. What can be the explanation other than that which I have indicated?—I am, etc.,

W. BASTIAN,
Surgeon Commander R.N.

H.M.S. *Victory*, Portsmouth, Nov. 20th.

SIR,—The prescription given in the letter on the treatment of fever in your issue of November 18th (p. 1000) was extensively used in the British Stationary Hospital, Baghdad.

It was used as an almost universal prescription in most of the fever cases admitted. Admissions numbered anything up to 35 per diem during the sandfly period of the year, and it invariably relieved the symptoms. To the first powder given on admission calomel gr. iv was added.

During one busy day a sergeant (R.A.F.) was admitted with typical symptoms of sandfly fever. I noted, however, that the pain in the back was more severe than usual; the temperature on the third day was normal, the chart being a typical one of sandfly fever. The above prescription was used. The following day he complained of heat rash. This struck me as peculiar, as his temperature was normal; on examining him I found him to be suffering from small-pox. His symptoms were only mild, and he was never very ill; he had never been vaccinated. This may have been due to the elimination of toxins through the skin in the early period of the disease. As he was sent to the isolation hospital the case was lost sight of; unfortunately just one month later, when convalescence was just established, he died suddenly, from what cause I do not know.

We got to believe in this prescription to such an extent that we invariably gave it to all heatstroke cases. During the hot weather of 1921 the percentage of deaths from heatstroke was much lower than it had been previously; whether this had anything to do with the administration of this prescription is, of course, an open question, but it certainly tends to give one faith in using it.—I am, etc.,

T. GELSTON ATKINS,
Captain R.A.M.C.

London, W.C., Nov. 23rd.

SIR,—I noted with considerable interest the joint letter of Surgeon Commander Parnell, Dr. Green, and Sir Archdall Reid. For several years I have employed an almost identical prescription with such general satisfaction that I sometimes accuse myself of using it almost as a placebo. The intention is very remote from this, and although its original use was in some degree empirical it had a liberal element of pharmacological justification. The prescription is very simple: Aspirin, pulv. ipecac. co.—āā gr. x. During the paroxysms of malaria its effect is extremely comforting and beneficial, as I demonstrated in a recent paper (*Medical Officer*, October 21st, 1922). In the prodromal stages of ordinary catarrhal colds and influenza it produces not only a sense of well-being but I am sure often stops further developments. In the notorious P.U.O. of active warfare days, which no doubt had a definite though unknown pathology, one found its use very satisfactory. In such cases as parotitis appearing as a metastatic effect following laparotomies I have seen marked relief. In short, in most febrile states, including the exanthemata, its effect is marked and valuable.

Whether its use is specific or purely palliative, as one is almost compelled to suppose, it is nevertheless a most useful simple combination. Pulv. ipecac. co. in doses of gr. x practically never induces emesis in adults.—I am, etc.,

DONALD BUCHANAN.

London, S.E., Nov. 18th.

THE SMALL-POX OUTBREAK AT POPLAR WORKHOUSE.

SIR,—Dr. C. S. Thomson, in his letter in the BRITISH MEDICAL JOURNAL for November 25th, says that:

> The "unmodified first case, in actual practice, would not be likely to oblige by walking right into the arms of a medical man. More than likely the sufferer would have visited forty or fifty public houses, churches, or cinemas," etc.

I suggest that Dr. Thomson is quite wrong. The unmodified case of small-pox, in my experience, is much too ill to visit places of entertainment, and if he does not go to the doctor he goes home to bed and sends for the doctor to come to him.

Dr. Thomson tells us that his prescription for preventing small-pox is "vaccination at infancy, revaccination at 12 to 14, and a third session at 21," with additional vaccinations as and when necessary. I quite admit that if such a prescription could be applied to the whole population, without exception, small-pox would be quite effectually controlled; but Dr. Thomson must know quite well that such a prescription never has been, is never likely to be, and indeed never could be applied in this or any other country. Moreover, granted that it could be applied, I venture to suggest that the premium to be paid (in the form of so much vaccination) is out of all proportion to the risk to be insured against. Why saturate forty-five millions of people, old and young, with vaccination when there is good reason to believe, from the experience of the past twenty years, that small-pox can be effectually controlled without it? As well advocate the repeated inoculation of the entire population of this country against enteric fever. Perhaps Dr. Thomson would do so, but few common-sense business men would think of listening to him.

As regards Dr. Stansfield's letter, he says that even if we got rid of the danger arising from modified small-pox in vaccinated subjects there would still remain a possibility of missed cases in naturally mild small-pox in unvaccinated persons. My answer to this is that naturally mild small-pox *tends to "breed true,"* and gives rise to a mild strain of small-pox with a negligible mortality (small-pox of this type is really not worth the fuss that is often made about it). Small-pox modified by vaccination, on the other hand, does not breed true, and, so far from giving rise to modified small-pox, it may and often does spread a very virulent form of the disease. Hence vaccinated (but incompletely protected) persons may be a far greater danger to their neighbours than the unvaccinated, under present-day conditions, are ever likely to be.

It is interesting to learn that all of the 22 fatal cases in the present outbreak had been vaccinated, presumably in infancy.

It does not look as if the neglect of infantile vaccination in the East End had had much to do with the present outbreak, certainly not with its fatality. On the other hand, if, as I suspect, the man who originated this disastrous outbreak had been vaccinated, and if the nature of his attack was not diagnosed because it had been "masked" by vaccination, then it would not be unreasonable to contend that not neglect of infantile vaccination, but the presence of it was responsible. This may seem a hard saying, but it may be true and worthy to be believed nevertheless.—I am, etc.,

Leicester, Nov. 27th. C. KILLICK MILLARD.

Obituary.

CHRISTOPHER VISE, M.D.,

Physician to the General Hospital, Tunbridge Wells.

DR. CHRISTOPHER VISE of Tunbridge Wells died on November 14th, aged 66. He was the son of Mr. Edward Vise, surgeon, of Holbeach, and received his medical education at University College, London, and the University of Durham, took the diploma of M.R.C.S.Eng. in 1880, and graduated M.B.Durh. in 1882 and M.D. in 1884. After serving as ophthalmic assistant at University College Hospital, house-physician to the Hospital for Consumption, Brompton, and assistant demonstrator of anatomy at the University of Durham, he became house-surgeon and secretary of the General Hospital, Tunbridge Wells, from 1882 to 1887, and in 1893 was appointed an honorary physician, which post he retained until his death. He was gazetted surgeon lieutenant to the old Kent Volunteer Battalion in 1893, and received the Territorial Decoration on completion of twenty years' service. During the first two years of the war he served with the rank of Major R.A.M.C. as medical officer to the 4th Battalion Queen's Own Royal West Kent Regiment and the 5th Battalion of the Buffs. During the last two years of the war he was in charge of military hospitals at Doncaster and Worksop, and concluded his period of war service on the headquarters staff of the northern command at York. On demobilization he returned to Tunbridge Wells and resumed his duties as senior physician at the General Hospital. He was a member of the Tunbridge Wells Division of the British Medical Association, and for many years honorary physician to the Convalescent Hospital for Children at Hawkenbury; latterly he was local referee to the War Pensions Committee. He took a great interest in freemasonry, and served in 1890 as Worshipful Master of the Holmesdale Lodge, with which he had been connected for forty years. He leaves a widow, a daughter, and three sons. His sons all passed through Tonbridge School with distinction, and two of them gained scholarships to Oxford.

Sir STCLAIR THOMSON sends us the following notes: Christopher Vise was my very oldest friend in the profession, for we both commenced our studies together in the now extinct stage of "apprentices." He and I were "pupils" in the Infirmary in Peterborough under the well-known Dr. Tom Walker, who was one of the most distinguished surgeons in the Midlands of his time; his name will go down in the history of laryngology as being the first in this country to remove a growth from a vocal cord, through the mouth, by the help of the laryngoscope. Vise represented the sixth generation of medical men in one family who had all practised in the south of Lincolnshire. He presented to the Medical Society of London during the year that I was President (1917) the patent of election of that body given to his great-grandfather. It is printed in Latin, dated "*Die Martis, 4to Augusti*, 1789," and is addressed to *Viro Celeberrimo Gulielmus Vyse, Chirurgo Praeses et Societas Medica Londinensis S.P.D.*" In his sterling character, genial manners, guileless nature, and unselfish service to friends and patients, Christopher Vise was a worthy descendant of this long line of medical men. His simple-hearted devotion to all his duties—private, professional, or civic—his unruffled temper, and his delightful urbanity, made everyone his friend. He lived to please and to be pleased, and all who knew him rejoice to think that he never made an enemy.

THE death took place on November 17th at Hampstead of Dr. JAMES ANDREWS, in his 93rd year. He was born at Pershore, and served, as was then the custom, an apprenticeship in his native town. In 1848 he entered as a student at Guy's Hospital. At this time Aston Key was at the height of his career, and Addison and Bright were active members of the staff. Dr. Andrews was dresser to Bransby Cooper, and after taking the diplomas of M.R.C.S. and L.S.A. in 1851, and the M.D.St. Andrews in 1854, commenced practice in the Camden Road. In 1872 he removed to Hampstead and continued in active practice there until his retirement in his 80th year. He knew and had interesting reminiscences of most of the great consultants of the last century, and his greatest admiration was for Sir Thomas Watson. To the last he retained all his faculties, and took a keen interest in modern developments both in medicine and public affairs. His son, Dr. E. Collingwood Andrews, is in practice at Hampstead.

WE regret to announce the death, in his 67th year, of Dr. DAVID MAVER, an esteemed country medical practitioner of Bucksburn, near Aberdeen. Dr. Maver graduated at Aberdeen University M.B., C.M. in 1878. Besides having an extensive practice in Bucksburn he had several parochial appointments, and was superintendent of the Summerfield Hospital. He was a justice of the peace for the county of Aberdeen and was also a member of the educational authority.

Universities and Colleges.

UNIVERSITY OF LONDON.

THE following candidates have been approved at the examination indicated:

DIPLOMA IN PSYCHOLOGICAL MEDICINE (*with special knowledge of Psychiatry*).—H. E. L. Canney, G. F. Cobb, R. D. Gillespie, D. I. O. Macaulay, D. Matthew, H. M. North, W. R. Page.

A course of five lectures on "The nature of ultramicroscopic viruses" will be given by Mr. F. W. Twort, superintendent of the Brown Institution, in the theatre of the Royal College of Surgeons, Lincoln's Inn Fields, W.C., on December 11th, 12th, 15th, 18th, and 19th, at 4 p.m. Admission will be free without ticket.

UNIVERSITY OF GLASGOW.

THE following appointments to bursaries are announced:

The Arthur (Medical) Bursary, value £20 for three years, to Mary G. Gorrie, who took the highest place among the Queen Margaret College candidates at the First Professional Examination held at the University.

Lorimer (Medical) Bursary, £25 for three years, William Scobie.

Rainy Bursary, £20 for two years, Morton A. Foulis; Monteith Bursary, £21 for two years, Raymond A. Currie; Davidson Bursary, £34 for three years, Robert B. Smith; Weir Bursary, £18 for one year, David Hynd, M.A.

ROYAL COLLEGE OF PHYSICIANS OF LONDON.

AN extraordinary Comitia of the Royal College of Physicians of London was held on Friday, November 24th, when the President, Sir Humphry Rolleston, was in the chair.

Licences to practise physic were granted to Cyril Rickwood Lane and Ella Kennedy Will.

Permission was granted to the Museum Galleries to photograph certain oil paintings in the possession of the College, and to the Dean of the Middlesex Hospital Medical School to have a copy made of the portrait of Sir Thomas Watson. It was agreed to lend to Mr. Percy Bigland (who painted it) the portrait of Sir Samuel Wilks, now in the College, for the purpose of exhibiting it at the Corporation Gallery Hall.

The resignation of Dr. R. A. Young of the office of Examiner on his appointment to the Committee of Management was accepted as from July, 1923.

The President announced that Dr. Kenneth N. G. Bailey has been appointed Streatfeild Research Scholar.

Dr. H. G. Turney was appointed Representative of the College on the Council of the Queen's Jubilee Fund for Nurses, vice Sir Dyce Duckworth, resigned.

Sir Humphry Rolleston was elected Representative of the College on the General Medical Council, vice Sir Norman Moore, resigned.

The Services.

DENTAL OFFICERS, R.N.

AT the recent examination of candidates for entry into the Royal Navy as dental officers, held at the Royal Dental Hospital of London, in November, the following qualified for appointment:

J. M. Park, L.D.S. (Glasgow); W. T. L. Douglas, L.D.S. (London); J. L. Edwards, L.D.S. (Liverpool); S. E. Brown, L.D.S. (Dublin).

The names are arranged in order of merit.

The fourth annual 19th Casualty Clearing Station dinner will be held at the Imperial Restaurant, 62, Regent Street, London, on Friday, December 15th. All who were active members of, or associated with, 19th C.C.S. are invited to attend. Tickets, 15s. exclusive of wine, may be obtained from the Rev. E. C. Doddnell, 6, Alexandra House, Regent's Park Road, Finchley, N.3.

Medical News.

A REUNION dinner of graduates and undergraduates of the Durham University College of Medicine will be held at the County Hotel, Newcastle-upon-Tyne, on Thursday, December 14th, at 7.30 p.m. The chair will be taken by Professor H. Brunton Angus, and the guest of the evening will be Mr. Cecil A. Cochrane, M.A., D.C.L. Applications for tickets (undergraduates 6s., graduates and others 12s. 6d.) should be sent to Mr. G. C. Parkin, College of Medicine, Newcastle-upon-Tyne, on or before December 6th.

SIR ARTHUR NEWSHOLME, K.C.B., M.D., will give two Chadwick lectures on relative values in public health at the Royal Society of Medicine on Thursdays, December 7th and 14th, at 5.15 p.m. on each day. Sir James Crichton-Browne will preside at the first lecture, which will deal with vital statistics, professional and popular education, and the influence of general sanitation, specific sanitation, and combined action. The second lecture, at which Mr. W. Addington Willis, a Chadwick trustee, will be in the chair, will deal with the degrees of preventability of disease and with financial questions.

THE annual dinner of the Epsomian Club will take place at the Trocadero Restaurant on Thursday, December 14th, at 7.30 p.m. The price of the dinner will be 12s. (exclusive of wine) and will be collected at the table. Any members intending to dine are requested to notify the honorary secretary, Mr. S. Maynard Smith, 49, Wimpole Street, W.1, as soon as possible, and to give the names of friends they wish to sit near so that table plans may be prepared.

PROFESSOR S. LYLE CUMMINS, C.B., will read a paper on "Acquired resistance to tuberculosis: a factor in clinical type and prognosis," at the meeting of the Bristol Medico-Chirurgical Society on Wednesday, December 13th, at 8 p.m. The meeting will be held in the medical library of the university. Dr. J. A. Nixon, C.M.G., president, will be in the chair.

THE King has appointed Dr. Percy James Kelly (Surgeon General) to be a member of the Executive Council of the Colony of British Guiana.

AT a meeting of the Association of Economic Biologists to be opened in the Botanical Department of the University of Manchester on Friday, December 15th, Dr. W. Lawrence Balls will introduce a discussion on genetics in relation to applied biology. After dinner (in the university refectory) informal discussions will take place on the place of applied biology in universities, and on the relation of biology to medicine. On Saturday a visit will be paid to the British Cotton Industry Research Association at Didsbury.

THE Industrial Fatigue Research Board has issued a report containing two documents, one, on the influence of temperature and other conditions on the frequency of industrial accidents, by Miss Ethel E. Osborne and Dr. H. M. Vernon, and the other, on the relation of fatigue and accuracy to speed and duration of work, by Mr. B. Muscio. We intend to publish a review of the report in an early issue.

THE annual dinner of the Chelsea Clinical Society was held on November 22nd at the Café Royal, with Dr. Campbell McClure, president of the society, in the chair. Sir Sydney Russell-Wells, in proposing the toast of "The Chelsea Clinical Society," pointed out the advantages of the smaller informal medical societies as contrasted with those which were larger and necessarily more formal. In the smaller societies it was better, he said, to discuss things freely without set papers, to discuss failures as well as successes, and to encourage the spirit of research rather than to have as their ambition volumes of printed transactions lying unread in some dusty library. Dr. Campbell McClure, in his reply, said that their society included men from all the many and varied branches of the medical profession. He emphasized the benefit that some years' experience of general practice gave to the specialist, and the value to the surgeon of having been a house-physician. It was a great advantage to the general practitioner to make a point of being present at operations on his own patients. The health of the guests was proposed with many compliments by Mr. Ivor Back. Sir Humphry Rolleston, President of the Royal College of Physicians, recalled, in reply, the many links between Chelsea and the Royal College of Physicians; Sir William Hale-White, President of the Royal Society of Medicine, also replied. The health of the chairman and officers of the society was proposed by Dr. Halls Dally, who stated that the society was never in a more prosperous condition than it was at present; Dr. Campbell McClure and Dr. Eckenstein (treasurer) replied. During the course of the evening some excellent songs were sung by Captain Radcliffe and by Mr. Norman Long.

THE Home Secretary gives notice under date November 24th that in view of the fact that the Dentists Act, 1921 (which prohibits the practice of dentistry by persons who are not registered dentists), comes into force on November 30th he has withdrawn as from the same date the special authority under the Dangerous Drugs Act, 1920, which was given to certain unregistered dentists to purchase local dental anaesthetics containing cocaine. On November 30th those unregistered dentists—if any—to whom the special authority applied, and whose names have not been put on the *Dental Register*, ceased to have any authority to be in possession of cocaine solutions, and should dispose forthwith of any stocks remaining in their possession to an authorized person.

THE third annual dinner and dance arranged by the Panel Committee for the County of London will take place on December 7th, at 7.30 p.m., at the Connaught Rooms, Great Queen Street, Kingsway, W.C.2. Tickets (gentlemen 21s., ladies 15s., exclusive of wine) may be obtained from Dr. Robert J. Farman, Staple House, 51, Chancery Lane, W.C.2. All practitioners will be welcomed. Carriages at 2 a.m.

THE annual dinner of the Medical Society of University College Hospital will take place on Tuesday, December 12th, at Gatti's Restaurant, Strand, at 7.30 p.m. Mr. T. H. Somervell, F.R.C.S., who was a member of the Mount Everest expedition, and has returned to England lately, will be the guest on this occasion. Tickets, 10s. 6d. each, may be obtained from the honorary secretary, J. A. Hadley, University College Hospital.

THE annual address before the Newcastle and Northern Counties Medical Society will be delivered on Thursday, December 7th, at 4.30 p.m., in the Physical Theatre, Armstrong College, by Sir Humphry Rolleston; the title of the address is "Some reflections on high arterial blood pressure." The annual dinner is to be held on the evening of the same day, when the guest will be Sir Humphry Rolleston.

AT a meeting of the Maternity and Child Welfare Group (Metropolitan and Home Counties) of the Society of Medical Officers of Health on Tuesday, December 12th, at 5.15 p.m., Mr. Eardley Holland will read a paper, well illustrated with lantern slides, on the dangers of breech presentation to foetal and infant life. The meeting is open to members of the medical profession.

Letters, Notes, and Answers.

As, owing to printing difficulties, the JOURNAL *must be sent to press earlier than hitherto, it is essential that communications intended for the current issue should be received by the first post on Tuesday, and lengthy documents on Monday.*

CORRESPONDENTS who wish notice to be taken of their communications should authenticate them with their names—of course not necessarily for publication.

AUTHORS desiring reprints of their articles published in the BRITISH MEDICAL JOURNAL are requested to communicate with the Office, 429, Strand, W.C.2, on receipt of proof.

IN order to avoid delay, it is particularly requested that ALL letters on the editorial business of the JOURNAL be addressed to the Editor at the Office of the JOURNAL.

THE postal address of the BRITISH MEDICAL ASSOCIATION and BRITISH MEDICAL JOURNAL is 429, Strand, London, W.C.2. The telegraphic addresses are:

1. EDITOR of the BRITISH MEDICAL JOURNAL, *Aitiology, Westrand, London*; telephone, 2630, Gerrard.
2. FINANCIAL SECRETARY AND BUSINESS MANAGER (Advertisements, etc.), *Articulate, Westrand, London*; telephone, 2630, Gerrard.
3. MEDICAL SECRETARY, *Medisecra, Westrand, London*; telephone, 2630, Gerrard.

The address of the Irish Office of the British Medical Association is 16, South Frederick Street, Dublin (telegrams: *Bacillus, Dublin*; telephone, 4737, Dublin), and of the Scottish Office, 6, Rutland Square, Edinburgh (telegrams: *Associate, Edinburgh*; telephone, 4361, Central).

QUERIES AND ANSWERS.

INCOME TAX.

"D. B. J. F." asks whether he can deduct as professional expenses a proportion of the rates, ground rent, and repairs of his leasehold house.

*** We assume that our correspondent has a consulting room and, probably, other professional accommodation at his residence. He is entitled to include in his professional expenses a reasonable proportion of the rates and repairs and of the net assessment to income tax, Schedule A, of the property. This latter deduction takes the place of a proportion of the ground rent.

"H. J. H." bought a secondhand 10-h.p. Singer in 1920 for £350, and sold it in 1922 for £80; in that year he purchased a new 10/15-h.p. Fiat for £735, claiming as an expense £735 – £80 = £655.

*** The amount allowable is £350 – £80 = £270 only; the balance of the expenditure—namely, £385—was incurred in improving, not merely in maintaining the equipment.

"W. G.'s" car transactions have been as follows:

1920.	Overland car bought for		£505
1922.	,, ,, sold for		£150
1922.	Rover ,, bought for		£550

The price of an Overland car similar to the one sold is understood to have been £268 when the Rover car was bought.

*** In our opinion "W. G." is entitled to claim the amount expended, provided that he does not increase the amount of capital sunk in his equipment. On that basis his allowance would be £505–£150=£355. We assume that the question is not complicated by his having received an allowance for the Overland car as an expense of 1920.

First Aid in Coal Mines.

"COLLIERY SURGEON" asks if there is anything published that could be of use, as far as the first aid attention to wounds is concerned, to the comparatively untrained attendant of a colliery ambulance room, who works under the colliery surgeon's weekly supervision.

A Strange "Wild-fowl."

DR. JAMES R. WHITWELL (Melton) writes: It is probable that this is one of the Ixodoid Acarinae which not infrequently attach themselves to any mammal, and are usually obtained from herbage of some kind. The description given, however, is insufficient for identification. They are to be found even in the high civilization of the Midlands!

DR. J. D. ROBSON (Dumfries) writes: I would suggest that Dr. F. G. Layton's strange "wild-fowl" was one of the Arachnids or ticks which infest sheep and sometimes dogs. Shepherds are often affected by them after sheep-shearing, and if the parasite gets itself well dug in it is no easy matter to remove it. Some time ago a child was brought me with one attached to the back of the neck, and it was so gorged with blood that it looked like a naevus until its movements gave it away.

SURGEON REAR-ADMIRAL W. EAMES, R.N., retd. (Bournemouth), writes: The strange "wild-fowl" would appear, from Dr. Frank G. Layton's account of the tenacious hold it had on the patient's skin, to be the ordinary sheep tick, which so frequently attaches itself to dogs moving in sheep-grazing areas, and the removal of which, owing to its extremely firm hold on the skin, causes, in some instances, much pain.

Warming the Garage.

DR. GEO. SMITH SOWDEN (Elgin) writes to recommend Brown Bros.' "Buckingham" radiator lamps. "I used one," he continues, "in a very cold part of the country all last winter, with excellent results. The lamp is constructed on the principle of the miner's safety lamp, and, when not used on the car, can be used as a garage light. Paraffin is the fuel to employ, and if the frost be very keen a rug thrown over lamp and radiator is quite sufficient." The cost of the lamp is 32s. 6d.

"ANOTHER ROVER" suggests the use of Davy colliery lamps—one, two, or three, according to the weather—under the bonnet, provided the garage is not draughty.

MESSRS. GAMAGE (Holborn, E.C.1) have on sale the Ever Warm radiator lamp, made on the principle of the miner's lamp, price 17s. 6d. It is recommended for warming garages.

LETTERS, NOTES, ETC.

Bad Arms after Vaccination.

WE publish in this issue under the title "The Art of Vaccination" (p. 1090) a statement which a very experienced public vaccinator has been good enough to write, giving the precautions which in his opinion should be taken to prevent the occurrence of "bad arms," and we may be able to recur to the subject in a future issue. Meanwhile we may say that Dr. Edgar J. Tyrrell (London, E.C.3) has written to recommend the local application of a 10 per cent. solution of glyco-thymoline if the arm is swollen and irritable.

The Violators of Vaccination Law.

DR. C. D. SOMERS, Public Vaccinator (Aldeburgh-on Sea), writes: Might I point out to Dr. H. P. Reynolds (November 18th, p. 1004) that all a J.P. has to do is to witness the signature of the application and has not to satisfy himself whether the applicant is a conscientious objector or not. If the applicant insists that he is, the J.P. cannot refuse to witness his signature. I used to think it was the fault of the J.P., but I no longer think so.

Removal of a Paper Fastener from the Bronchus.

MR. E. MUSGRAVE WOODMAN, F.R.C.S. (Birmingham), writes: I congratulate Mr. Herbert Tilley not less on the successful issue of his case than on the polished English of his article. Only those accustomed to work in the dismal and dark recesses of these tubes can fully appreciate the difficulties that may be met with. Not the least of these is the impossibility of having at hand the right instrument for each particular case—in regard both to length and to forceps ends. I sympathize with the words of Chevalier Jackson: "When I have fully diagnosed a case I go into my workshop and make an instrument of appropriate length and design for the work it has to do." One thing I am sure of: Mr. Tilley need make no apology for the use of general anaesthesia. We in this country are blessed by the help of anaesthetists trained to an extent not often found either in Europe or America. I think that general anaesthesia will always be the method of choice in this country.

The Determination of Sex.

DR. J. WEST (Ramna, Dacca, Bengal) writes: Dr. R. W. Marsden, in your issue of September 30th, 1922 (p. 616), brings forward a new theory regarding the determining factors in the production of sex in man. During the past six years from time to time letters have appeared discussing this subject. This has caused me some surprise, and at times some confusion. I was on the point of writing to inquire whether the theory expressed sufficiently definitely by E. G. Conklin of Princeton University (*Heredity and Environment in the Development of Man*, Oxford University Press, 1915) was not generally accepted as regards man, since these frequent revivals of the "problem" appeared to ignore it. It so happened, however, that before I had carried out my intention the mail brought in the 1922 edition of this book, in which I read on page 166: "These discoveries appear to settle once for all this vexing question and to establish the *fact* that in man, as well as in many other animals, sex is determined . . ." Instead of completing the quotation I prefer to refer your correspondent to the original work.

Pluriglandular Tablets.

"B." writes, in reply to "Stratford": I have taken tetraglandular tablets (P. D. and Co.) for about three years—present age, 61. I take one in the morning and another in the afternoon. They are markedly restorative when one feels tired, and have no ill effects. They do not tend to preserve the eyesight, however, nor help a cardiac murmur. I propose to try hexaglandular tablets for a while. When bicycling and climbing in Switzerland this summer I found that children of 16 were greatly helped by such a "tetra" tablet when tired, though the effect soon wore off.

Scopolamine-Morphine during Labour: Correction.

DR. N. HIRSCHMAN calls attention to an error of dosage printed in his paper on the "standardized-dosage" method of using scopolamine-morphine during labour (BRITISH MEDICAL JOURNAL, October 14th, 1922). Under "Results" (p. 670, col. 2) the first two lines of Series I should read as follows: "The cases in this series had an initial dose of 2/3 grain omnopon and 1/150 grain scopolamine, with an hourly injection of 1/450 grain scopolamine."

A Pharmacist's Oath.

DR. ROLAND GUÉBHARD (St.-Cézaire) has recently sent to *La Chronique Médicale* a copy of the oath taken by pharmacists in France in the seventeenth century. It may be freely translated as follows:

> I swear before God, the author and creator of all things, to respect and serve as well as in me is, not only the doctors of medicine who have given me instruction in pharmacy, but also my pharmacist teachers under whom I have learnt.
>
> Not to speak evil of my former doctors, pharmacist teachers, or any other persons, whoever they may be.
>
> To do all that I possibly can for the glory, honour, ornament, and dignity of the profession.
>
> Not to teach its secrets and curiosities to idiots or unsuitable persons.
>
> Not to do anything rashly without the advice of doctors.
>
> To conduct myself properly with women when it is necessary to apply a remedy, and never to give any kind of poison to any person.

Vacancies.

NOTIFICATIONS of offices vacant in universities, medical colleges, and of vacant resident and other appointments at hospitals, will be found at pages 29, 32, 33, and 34 of our advertisement columns, and advertisements as to partnerships, assistantships, and locumtenencies at pages 30 and 31.

A short summary of vacant posts notified in the advertisement columns appears in the *Supplement* at page *203*.

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